# **WEST Search History**

Hide Items Restore Clear Cancel

DATE: Wednesday, October 27, 2004

Hide?	Set Name	Query	<u>Hit</u> Count
	DB=P	GPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
	L31	L30 AND nestin	48
	L30	L29 NOT Rosen-Craig-A.IN.	336
	L29	L28 AND 435/325.CCLS.	483
	L28	L27 AND L25	1261
	L27	astrocyte	4700
	L26	L22 AND L25	189
	L25	aFGF OR bFGF OR FGF-1 OR FGF-2 OR acidic FGF OR basic FGF OR amphiregulin OR EGF OT TGFa OR TGFalpha	8001
	L24	FGF OR TGF	18811
	L23	L22 AND adhesion	132
	L22	nestin AND GFAP	252
	L21	L20 AND adhesion	93
	L20	L19 NOT Rosen-Craig-A.IN.	166
	L19	L18 AND human	167
	L18	L17 AND GFAP	167
	L17	L16 AND nestin	257
	L16	435/325,366,368,378.CCLS.	17391
	L15	Wictorin.IN.	6
	L14	Wictorin-K.IN.	1
	L13	Wictorin-Klas.IN.	0
	L12	Eriksson.IN.	3788
	L11	Eriksson-C.IN.	. 27
	L10	Eriksson-Cecilia.IN.	0
	L9	Skoijh.IN.	0
	L8	Skoijh-C.IN.	0
	L7	Skoijh-Charlotta.IN.	0
	L6	Campbell.IN.	20686
	L5	Campbell-K.IN.	19
	L4	Campbell-Kenneth.IN.	5
	L3	Wahlberg.IN.	526
	L2	Wahlberg-L.IN.	10
	L1	(Wahlberg-Lars. IN.)	11

# **Hit List**

Clear Generate Collection Print Fwd Refs Bkwd Refs Generate OACS

## Search Results - Record(s) 1 through 11 of 11 returned.

☐ 1. Document ID: US 5643773 A

Using default format because multiple data bases are involved.

L1: Entry 1 of 11

File: USPT

Jul 1, 1997

US-PAT-NO: 5643773

DOCUMENT-IDENTIFIER: US 5643773 A

TITLE: Preparation of elongated seamless capsules containing a coaxial rod and

biological material

DATE-ISSUED: July 1, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Aebischer; Patrick Barrington RI Mills; John F. Wakefield RI Wahlberg; Lars Providence RI Doherty; Edward J. Mansfield MA

Tresco; Patrick A. Salt Lake City UT

US-CL-CURRENT: 435/182; 264/4, 264/4.7, 424/451, 425/382R, 425/382.2, 435/178, 435/179, 435/325, 435/368, 435/382, 530/817

Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	KMC Draw Desc

☐ 2. Document ID: US 5418154 A

L1: Entry 2 of 11

File: USPT

May 23, 1995

US-PAT-NO: 5418154

DOCUMENT-IDENTIFIER: US 5418154 A

TITLE: Method of preparing elongated seamless capsules containing biological material

DATE-ISSUED: May 23, 1995

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Aebischer; Patrick Barrington RI
Mills; John F. Wakefield RI
Wahlberg; Lars Providence RI

Doherty; Edward J. Mansfield MA

Tresco; Patrick A. Salt Lake City UT

US-CL-CURRENT:  $\underline{435/182}$ ;  $\underline{264/4}$ ,  $\underline{264/4.7}$ ,  $\underline{424/451}$ ,  $\underline{425/382R}$ ,  $\underline{425/382.2}$ ,  $\underline{435/178}$ ,

435/179, 530/817

#### ABSTRACT:

Elongated seamless capsules containing biological material are prepared by a method in which a coagulant, which includes a cell suspension or other biologically active factor, and a polymeric casting solution are extruded through a common extrusion port having at least two concentric bores, such that the coagulant is extruded through the inner bore and the polymeric casting solution is extruded through the outer bore. The method involves initiating extrusion of the coagulant subsequent to initiating delivery of the casting solution through the respective bores to form a capsule having a curved and smooth leading edge shape. Delivery of the coagulant is then shut off, and extrusion of the casting solution is terminated either immediately or after some predetermined time.

31 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 8

Full Title Citation Front Review Classification	Date Reference	Claims KMC Draw Desi
☐ 3. Document ID: US 5389535 A		
L1: Entry 3 of 11	File: USPT	Feb 14, 1995

US-PAT-NO: 5389535

DOCUMENT-IDENTIFIER: US 5389535 A

TITLE: Method of encapsulating cells in a tubular extrudate

DATE-ISSUED: February 14, 1995

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Aebischer; Patrick Barrington RI

Wahlberg; Lars Gavle SE

US-CL-CURRENT:  $\underline{435/182}$ ;  $\underline{264/4}$ ,  $\underline{264/4.7}$ ,  $\underline{425/382R}$ ,  $\underline{435/179}$ ,  $\underline{435/180}$ ,  $\underline{435/297.1}$ ,

435/382

## ABSTRACT:

Methods and systems are disclosed for encapsulating viable cells which produce biologically-active factors. The cells are encapsulated within a semipermeable, polymeric membrane by co-extruding an aqueous cell suspension and a polymeric solution through a common port to form a tubular extrudate having a polymeric outer coating which encapsulates the cell suspension. For example, the cell suspension and the polymeric solution can be extruded through a common extrusion port having at least two concentric bores, such that the cell suspension is extruded through the inner bore and the polymeric solution is extruded through the outer bore. The polymeric solution coagulates to form an outer coating. As the outer coating is formed, the ends of the tubular extrudate can be sealed to form a cell capsule. In one embodiment, the tubular extrudate is sealed at intervals to define separate cell compartments connected by polymeric links.

20 Claims, 8 Drawing figures

Claims KWC Draw Des

## ☐ 4. Document ID: US 5284761 A

L1: Entry 4 of 11

File: USPT

Feb 8, 1994

US-PAT-NO: 5284761

DOCUMENT-IDENTIFIER: US 5284761 A

\*\* See image for Certificate of Correction \*\*

TITLE: Method of encapsulating cells in a tubular extrudate

Full Title Citation Front Review Classification Date Reference

DATE-ISSUED: February 8, 1994

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Aebischer; Patrick

Barrington

RI

SE

Wahlberg; Lars

Gavle

US-CL-CURRENT: 435/182; 425/382R, 435/179, 435/180, 435/382

## ABSTRACT:

Methods and systems are disclosed for encapsulating viable cells which produce biologically-active factors. The cells are encapsulated within a semipermeable, polymeric membrane by co-extruding an aqueous cell suspension and a polymeric solution through a common port to form a tubular extrudate having a polymeric outer coating which encapsulates the cell suspension. For example, the cell suspension and the polymeric solution can be extruded through a common extrusion port having at least two concentric bores, such that the cell suspension is extruded through the inner bore and the polymeric solution is extruded through the outer bore. The polymeric solution coagulates to form an outer coating. As the outer coating is formed, the ends of the tubular extrudate can be sealed to form a cell capsule. In one embodiment, the tubular extrudate is sealed at intervals to define separate cell compartments connected by polymeric links.

16 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Front Review Classification	Date Reference		KMC	Draw, Desi
☐ 5. Document ID: US 5283187 A L1: Entry 5 of 11	File: USPT		1,	1994

US-PAT-NO: 5283187

DOCUMENT-IDENTIFIER: US 5283187 A

\*\* See image for Certificate of Correction \*\*

TITLE: Cell culture-containing tubular capsule produced by co-extrusion

DATE-ISSUED: February 1, 1994

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Aebischer; Patrick Barrington RI

Wahlberg; Lars Gavle SE

US-CL-CURRENT: 435/182; 435/179, 435/325

### ABSTRACT:

Living cells such as animal cells which produce biologically active factors are encapsulated within a semipermeable, polymeric membrane such as polyacrylate by coextruding an aqueous cell suspension and a polymeric solution through a common port having at least one concentric bores to form a tubular extrudate having a polymeric membrane which encapsulates the cell suspension. The cell suspension is extruded through an inner bore and the polymeric solution is extruded through an outer bore while a pressure differential is maintained between the cell suspension and the polymeric solution to impede solvent diffusion from the polymeric solution into the cell suspension. The polymeric solution coagulates to form an outer coating or membrane as the polymeric solution and the cell suspension are extruded through the extrusion port. As the outer membrane is formed, the ends of the tubular extrudate are sealed to form a cell capsule. In one embodiment, the tubular extrudate is sealed at intervals to define separate cell compartments connected by polymeric links. In another embodiment, a cell capsule connected to a tethering filament is formed. The polymeric membrane may contain additives such as a surfactant, an anti-inflammatory agent or an anti-oxidant and can be coated with a protective barrier. The cell suspension may contain nutrients and an anchorage substrate.

20 Claims, 9 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Front Review Classifica	ation Date Reference	Claims KMMC Draw Desc
	······································	
☐ 6. Document ID: US 5158881	A	
L1: Entry 6 of 11	File: USPT	Oct 27, 1992

US-PAT-NO: 5158881

DOCUMENT-IDENTIFIER: US 5158881 A

TITLE: Method and system for encapsulating cells in a tubular extrudate in separate

cell compartments

DATE-ISSUED: October 27, 1992

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Aebischer; Patrick Barrington RI

Wahlberg: Lars Gavle SE

US-CL-CURRENT: 435/182; 425/382R, 435/179, 435/180, 435/382

ABSTRACT:

Methods and systems are disclosed for encapsulating viable cells which produce biologically-active factors. The cells are encapsulated within a semipermeable, polymeric membrane by co-extruding an aqueous cell suspension and a polymeric solution through a common port to form a tubular extrudate having a polymeric outer coating which encapsulates the cell suspension. For example, the cell suspension and the polymeric solution can be extruded through a common extrusion port having at least two concentric bores, such that the cell suspension is extruded through the inner bore and the polymeric solution is extruded through the outer bore. The polymeric solution coagulates to form an outer coating. As the outer coating is formed, the ends of the tubular extrudate can be sealed to form a cell capsule. In one embodiment, the tubular extrudate is sealed at intervals to define separate cell compartments connected by polymeric links.

25 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Front Review Classification Date Reference Claims KMC Draw. Desc

☐ 7. Document ID: US D265630 S

L1: Entry 7 of 11

File: USPT

Aug 3, 1982

US-PAT-NO: D265630

DOCUMENT-IDENTIFIER: US D265630 S

TITLE: Cardboard box for packing and display

DATE-ISSUED: August 3, 1982

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Wahlberg; Birgitta S-755 90 Uppsala SE

Wahlberg; Lars S-755 90 Uppsala SE

US-CL-CURRENT: D09/456; D09/432

1 Claims, 4 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

Full Title Citation Front Review Classification Date Reference Claims KMC Draw Described By Branch B

File: EPAB

PUB-NO: WO003018779A1

L1: Entry 8 of 11

DOCUMENT-IDENTIFIER: WO 3018779 A1

TITLE: ISOLATION OF CELLS FROM NEURAL CELL POPULATIONS USING ANTIBODIES TO FA1/DLK1

PUBN-DATE: March 6, 2003

INVENTOR-INFORMATION:

Mar 6, 2003

NAME COUNTRY

JENSEN, CHARLOTTE HARKEN

TEISNER, BOERGE

DK

GROENBORG, METTE

DK

WAHLBERG, LARS

DK

INT-CL (IPC): C12 N 5/00; A61 K 35/30; C12 Q 1/00

EUR-CL (EPC): C12N005/06

#### ABSTRACT:

CHG DATE=20030507 STATUS=0>The present invention relates to the use of antibodies recognising Fetal Antigen-1 (FA1/dlk1) for the detection and isolation of cell subpopulations from neural cell populations, in particular from cell populations from the central nervous system. In one embodiment, the dopaminergic neurons in the Substantia nigra pars compacta are detected and separated from other cell populations in this region of the brain. In another embodiment, neural stem and progenitor cells are isolated from other more committed cells in the CNS. The isolated cells may be used for transplantation, drug screening, production of cell type specific antibodies, and gene discovery.

	sification Date Reference	
☐ 9. Document ID: WO 2086	106 A1	
L1: Entry 9 of 11	File: EPAB	oct 31, 2002

PUB-NO: WO002086106A1

DOCUMENT-IDENTIFIER: WO 2086106 A1

TITLE: METHOD AND CULTURE MEDIUM FOR PRODUCING NEURAL CELLS EXPRESSING TYROSINE

HYDROXYLASE

PUBN-DATE: October 31, 2002

INVENTOR-INFORMATION:

NAME COUNTRY
MEIJER, XIA 'SE
GROENBORG, METTE DK
WAHLBERG, LARS DK

INT-CL (IPC): C12 N 5/08; C12 N 5/06; C12 N 5/02; A61 K 35/30; A61 P 25/00

EUR-CL (EPC): C12N005/06; C12N005/06

### ABSTRACT:

CHG DATE=20030114 STATUS=0>The invention provides a method for efficiently generating large numbers of tyrosine hydroxylase (TH) expressing neural cells for neurotransplantation into a host to treat neurodegenerative disease, neurological trauma, stroke, or in other diseases of the nervous system involving loss of neural cells, particularly Parkinson's disease. The method comprises introducing a population of expanded and plated neural progenitor cells to a defined culture medium comprising one or more growth factors belonging to the fibroblast growth factor (FGF) family, a molecule which results in the activation of cyclic AMP (cAMP) dependent protein kinase (PKA) and an agent which activates protein kinase C (PKC).

## ☐ 10. Document ID: WO 9300063 A1

L1: Entry 10 of 11

File: EPAB

Jan 7, 1993

PUB-NO: WO009300063A1

DOCUMENT-IDENTIFIER: WO 9300063 A1 TITLE: CAPSULE EXTRUSION SYSTEMS

PUBN-DATE: January 7, 1993

INVENTOR-INFORMATION:

COUNTRY NAME US AEBISCHER, PATRICK US MILLS, JOHN F US WAHLBERG, LARS US DOHERTY, EDWARD J

INT-CL (IPC): A61J 3/00

EUR-CL (EPC): A61K009/00; B01J013/02, C12N005/06 , C12N011/04 , A61J003/07 ,

B01J013/04 , A61K009/50 , C12N005/06

## ABSTRACT:

CHG DATE=19990617 STATUS=0>Methods for producing cell capsules are disclosed in which a coagulant (22), which can include a cell suspension or other biologically active factor, and a polymeric casting solution (26) are extruded through a common extrusion port (14) having at least two concentric bores, such that the coagulant is extruded through the inner bore (16) and the polymeric casting solution is extruded through the outer bore (18). The method involves initiating extrusion of the coagulant within a temporal range of about 10 msecs to about one second from initiating delivery of the casting solution through the respective bores. Delivery of the coagulant is then shut off, and extrusion of the casting solution is terminated either immediately or after some predetermined time.

Full Title	Citation Front Review	Classification Date	Reference		Claims	KMMC Draw. D	:57
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□ 11.	Document ID: WO	9110425 A1					

File: EPAB

L1: Entry 11 of 11

PUB-NO: WO009110425A1

DOCUMENT-IDENTIFIER: WO 9110425 A1 TITLE: CELL CAPSULE EXTRUSION SYSTEMS

PUBN-DATE: July 25, 1991

INVENTOR-INFORMATION:

COUNTRY NAME US

AEBISCHER, PATRICK

Jul 25, 1991

WAHLBERG, LARS SE

US-CL-CURRENT: 435/182

INT-CL (IPC): A61K 9/50; B01J 13/04; C12N 11/04

EUR-CL (EPC): A61K009/00; A61K009/48, A61K009/48, B01J013/02, B01J013/04,

C12N005/06 , C12N005/06 , C12N011/04 , C12N011/08

### ABSTRACT:

CHG DATE=19990617 STATUS=O>Living cells (56) which produce biologically active factors can be encapsulated within a semipermeable, polymeric membrane by coextruding an aqueous cell suspension (54) and a polymeric solution (52) through a common port (14) to form a tubular extrudate (12) having a polymeric membrane which encapsulates the cell suspension. For example, the cell suspension and the polymeric solution can be extruded through a common extrusion port having at least two concentric bores (16 and 18), such that the cell suspension is extruded through the inner bore (16) and the polymeric solution is extruded through the outer bore (18). The polymeric solution coagulates to form an outer coating or membrane. As the outer membrane is formed, the ends of the tubular extrudate can be sealed to form a cell capsule. In one embodiment, the tubular extrudate is sealed at intervals to define separate cell compartments connected by polymeric links (58). In another embodiment, a cell capsule connected to a tethering filament (59) can be formed.

Full Title Citation Front Review	Classification Dat	te Reference		Claims KMC Draw, Des
Clear Generate Collection	Print	Fwd Refs	Bkwd Refs	Generate OACS
Terms			Documents	
(Wahlberg-Lars.IN.)				11

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## Search Results - Record(s) 1 through 10 of 10 returned.

# ☐ 1. Document ID: AU 2002325203 A1, WO 2003018779 A1, EP 1421179 A1

# Using default format because multiple data bases are involved.

L2: Entry 1 of 10

File: DWPI

Mar 10, 2003

DERWENT-ACC-NO: 2003-290066

DERWENT-WEEK: 200452

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TITLE: Obtaining cell populations enriched or diminished in Fetal Antigen-1 (FA1) expressing cells for use in transplantation, drug screening or gene analysis, by combining a population of mammalian neural cells with anti-FA1 antibodies

INVENTOR: GRONBORG, M; JENSEN, C H; TEISNER, B; WAHLBERG, L

PRIORITY-DATA: 2001US-314794P (August 24, 2001)

PATENT-FAMILY:

LANGUAGE PAGES MATN-TPC PUB-DATE PUB-NO 000 C12N005/00 March 10, 2003 AU 2002325203 A1 C12N005/00 March 6, 2003 047 F. WO 2003018779 A1 C12N005/00 000 EP 1421179 A1 May 26, 2004

INT-CL (IPC): A61 K 35/30; C12 N 5/00; C12 Q 1/00

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II	T:41 =	Chiadian.	Front	Passiana	Classification	Data	Reference	Claims KOMC Draw, De	₹ .
6.61	11111	CHAROLL	FIGURE	17 GAIGAA	Classification	Para	Treneralise.		_

Document ID: AU 2002302354 A1, WO 200286106 A1, EP 1385938 A1

L2: Entry 2 of 10

File: DWPI

Nov 5, 2002

DERWENT-ACC-NO: 2003-075628

DERWENT-WEEK: 200433

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TITLE: Producing neural cells expressing tyrosine hydroxylase for neurotransplantation into host to treat neurodegenerative disease, by expanding and plating neural progenitor cells in defined culture medium

INVENTOR: GRONBORG, M; MEIJER, X; WAHLBERG, L

PRIORITY-DATA: 2001US-289933P (May 9, 2001), 2001US-286084P (April 23, 2001)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 AU 2002302354 A1
 November 5, 2002
 000
 C12N005/08

 WO 200286106 A1
 October 31, 2002
 E
 044
 C12N005/08

INT-CL (IPC): A61 K 35/30; A61 P 25/00; C12 N 5/02; C12 N 5/06; C12 N 5/08

ABSTRACTED-PUB-NO: WO 200286106A

BASIC-ABSTRACT:

EP 1385938 A1

NOVELTY - Producing a population of neural cells expressing tyrosine hydroxylase (TH), involves expanding a population of neural progenitor cells (NPC), plating on a substrate (II) and introducing it into a defined culture medium (III) having growth factor(s) (IV), a molecule (V) that increases intracellular cyclic AMP (cAMP) and an agent (VI) that stimulates protein kinase C (PKC).

E

DETAILED DESCRIPTION - Producing a population of neural cells in vitro where a percentage of the cells express tyrosine hydroxylase (TH), involves expanding a population of neural progenitor cells (NPC), plating the population on a substrate (II) and introducing it into a defined culture medium (III) having growth factor(s) (IV) of fibroblast growth factor (FGF), molecule (V) that increases intracellular cyclic AMP (cAMP) and agent (VI) that stimulates protein kinase C (PKC).

INDEPENDENT CLAIMS are also included for the following:

- (1) a composition (I) produced by the above method;
- (2) reseeding (I) by trypsinization and seeding of the TH expressing cells; and
- (3) a defined culture medium described as above.

ACTIVITY - Antiparkinsonian; Cerebroprotective; Vulnerary; Tranquilizer.

MECHANISM OF ACTION - Cell therapy.

No biological data is given.

USE - (I) Is useful for treating a mammal with a tyrosine hydroxylase-related deficiency or a disease of the central nervous system (CNS) (e.g. neurodegenerative disease, neurological trauma, stroke and loss of neural cells), especially Parkinson's disease. (I) Is also useful for drug screening, gene expression analysis, for investigating a biochemistry and molecular mechanisms of NPC differentiation, for identifying compounds or genes involved in the induction of progenitor cell differentiation, and for the manufacture of a pharmaceutical for treating CNS diseases. (I) Is further useful for producing antibodies against TH expressing cells, which are useful for screening, identification, isolation and/or cell sorting of biological samples for TH expressing cells (claimed).

ADVANTAGE - The method efficiently generates large numbers of TH expressing neural cells.

Full   Title   Citation   Front   Review   Classification   Da	ste Reference	Claims KWMC Draw Desi
☐ 3. Document ID: SE 200101436 A L2: Entry 3 of 10	File: DWPI	Oct 25, 2002

DERWENT-ACC-NO: 2003-118946

DERWENT-WEEK: 200311

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TITLE: Stocking coaxial structure involves self-locking arrangement at one or both ends, enabling seams, legs and thread runs to be joined together without sewing

INVENTOR: WAHLBERG, L

PRIORITY-DATA: 2001SE-0001436 (April 24, 2001)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

SE 200101436 A

October 25, 2002

001

A61F002/00

INT-CL (IPC):  $A61 \pm 2/00$ 

ABSTRACTED-PUB-NO: SE 200101436A

BASIC-ABSTRACT:

NOVELTY - The stocking coaxial structure involves a self-locking arrangement at one or both ends, enabling seams, legs and thread runs to be joined together without sewing.

USE - As a self-locking arrangement for a stocking coaxial structure.

ADVANTAGE - The arrangement provides for greater strength and flexibility on the basis of the increased number of threads joined together in comparison with the conventional sewing process.

DESCRIPTION OF DRAWING(S) - The figure illustrates a section of a stocking.

Full   Title   Citation   Front   Review	o Classification Date Reference	u Des
		*************

## 4. Document ID: WO 200205644 A1, AU 200171223 A, SE 200002716 A

L2: Entry 4 of 10

File: DWPI

Jan 24, 2002

DERWENT-ACC-NO: 2002-171746

DERWENT-WEEK: 200236

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TITLE: Use of insulin, insulin like substances and/or degradation products for

preparation of a composition against blood sucking or biting insects

INVENTOR: FURBERG, B; MARD, J; WAHLBERG, L; MARDH, J

PRIORITY-DATA: 2000SE-0002716 (July 18, 2000)

PATENT-FAMILY:

MAIN-IPC LANGUAGE PAGES PUB-NO PUB-DATE 019 A01N037/44 January 24, 2002 WO 200205644 A1 A01N037/44 000 January 30, 2002 AU 200171223 A A01N037/44 000 January 19, 2002 SE 200002716 A

INT-CL (IPC): A01 N 37/44; A01 N 61/00; A01 N 63/00; A61 K 7/40

ABSTRACTED-PUB-NO: WO 200205644A

BASIC-ABSTRACT:

NOVELTY - A composition comprises insulin, insulin like substances and/or degradation products.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of insulin or

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.3&ref=2&dbname=PGPB,USPT,USO... 10/27/04

insulin like substances and degradation products for the preparation of the composition.

ACTIVITY - Insecticide.

No biological data given.

MECHANISM OF ACTION - None given.

USE - Against blood sucking or biting insects e.g. mosquitoes, flies, ticks, fleas, lice and ants.

ADVANTAGE - The composition prevents biting, sticking and blood sucking insects from attacking the human or animal body.

Full   Title   Citation   Front   Review   Classification   Date   Reference	

# 5. Document ID: EP 1228195 A1, WO 200130981 A1, AU 200111692 A

L2: Entry 5 of 10

File: DWPI

Aug 7, 2002

DERWENT-ACC-NO: 2001-335700

DERWENT-WEEK: 200259

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TITLE: New in vitro adhesion culture of glial fibrillary acidic protein immunoreactive (GFAP positive) cells useful for proliferating and differentiating GFAP positive nestin positive cells for transplantation to patients with Parkinson's disease

INVENTOR: CAMPBELL, K; ERIKSSON, C; FAGERSTROM, C; WAHLBERG, L; WICTORIN, K

PRIORITY-DATA: 2000US-0161316 (October 24, 2000), 1999US-161316P (October 25, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1228195 A1	August 7, 2002	Ε .	000	C12N005/06
WO 200130981 A1	May 3, 2001	E	064	C12N005/06
AU 200111692 A	May 8, 2001		000	C12N005/06

INT-CL (IPC): A61  $\times$  35/30; A61  $\times$  48/00; C12  $\times$  5/06; C12  $\times$  5/08; C12  $\times$  5/10; C12  $\times$  5/16; G01  $\times$  33/48

ABSTRACTED-PUB-NO: WO 200130981A BASIC-ABSTRACT:

NOVELTY - An in vitro adhesion cell culture of glial fibrillary acidic protein immunoreactive (GFAP+) cells, is new.

DETAILED DESCRIPTION - An in vitro adhesion cell culture GFAP+ cells, where:

- (a) one or more cells in the culture have the capacity to differentiate into neurones;
- (b) the cell culture divides in a culture medium containing serum (S) and at least one proliferation-inducing growth factor (PGF), and
- (c) one or more cells (I) in the culture have the capacity to differentiate into neurons, upon withdrawal of both (S) and PGF.

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INDEPENDENT CLAIMS are also included for the following:

- (1) an in vitro cell culture (I) consisting essentially of a culture medium containing (S) and PGF, and cells derived from the central nervous system of a mammal, where the cells in the culture are GFAP+, capable of proliferating in a culture medium containing (S) and PGF, and capable of differentiating into neurons in the absence of both the (S) and PGF from the culture medium;
- (2) producing (P1) a neuronal cell in vitro, by obtaining neural tissue from a mammal, the neural tissue containing at least one GFAP+ cell capable of producing progeny that is a GFAP+ cell, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate GFAP+ cell and produce a GFAP+ cell progeny, and differentiating the cell progeny in a second culture medium that is substantially free of both the (S) and PGF;
- (3) producing (P2) a non-neuronal cell in vitro, by P1, and differentiating the cell progeny in a second culture medium that is substantially free of (S);
- (4) producing (P3) a genetically modified GFAP+ cell, by P1, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (5) producing (P4) a genetically modified differentiated neural cell culture, by P1, and differentiating the cell progeny to contain at least 10% neurons in a second culture medium that is substantially free of both the (S) and PGF, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (6) producing (P5) a genetically modified non-neuronal cell culture, by P1, and differentiating the cell progeny to contain at least 10% glia in a second culture medium that is substantially free of (S), where the glia are GFAP+ and vimentin positive, and genetically modifying the non-neuronal cell;
- (7) transplanting GFAP+ nestin+ cell progeny to a host, by obtaining neural tissue from a mammal, the neural tissue containing at least one GFAP+ nestin+ cell capable of producing progeny that are capable of differentiating into neurons and glia, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ nestin+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate the GFAP+ nestin+ cell and produce GFAP+ nestin+ cell progeny, and transplanting the GFAP+ nestin+ cell progeny to the host;
- (8) determining the effect of at least one biological agent on a GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell progeny by the above said method, contacting the proliferated GFAP+ nestin+ cell with the biological agent, and determining the effect of biological agent on GFAP+ nestin+ cells;
- (9) determining the effect of at least one biological agent on the differentiation of GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said method, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate in a second culture medium in the presence of biological agent, and determining the effects of the biological agent on the differentiation of the GFAP+ nestin+ cells;
- (10) determining the effect of at least one biological agent on the differentiated GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said process, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate into neurons or glia, contacting the differentiated neural cells with the biological agent, and determining the effects of the biological agent on the differentiated neural cells;
- (11) a cDNA library prepared from (I); and
- (12) a cell population consisting essentially of isolated GFAP+ nestin+ cells.

ACTIVITY - Immunosuppressive; antiparkinsonian.

No supporting biological data given.

MECHANISM OF ACTION - None given.

USE - The culture method is useful for proliferating and differentiating GFAP+ nestin+ cells (claimed). The cultured cells are useful for transplantation procedures, particularly to patients suffering from Parkinsonian's disease.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KMC | Draw Description | Claims | Claims | KMC | Draw Description | Claims | Cla

DERWENT-ACC-NO: 1997-350244

DERWENT-WEEK: 199837

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TITLE: Integrally formed seamless capsules - are suitable for encapsulation of biological materials

INVENTOR: AEBISCHER, P; DOHERTY, E J; MILLS, J F; TRESCO, P A; WAHLBERG, L

PRIORITY-DATA: 1992US-0997770 (December 24, 1992), 1987US-0121626 (November 17, 1987), 1990US-0461999 (January 8, 1990), 1991US-0638759 (January 8, 1991), 1991US-0722852 (June 28, 1991), 1995US-0430786 (April 27, 1995)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 US 5643773 A
 July 1, 1997
 E
 019
 C12N011/04

INT-CL (IPC): A61 K 9/48; B01 J 13/02; C12 N 5/00; C12 N 11/04

ABSTRACTED-PUB-NO: US 5643773A

BASIC-ABSTRACT:

Method for integrally forming an elongated seamless capsule is new.

The capsule contains a coaxial rod which is connected only to one end of the capsule.

The capsule is formed by:

- (a) extruding a casting solution through an outer bore of a multiple annular extrusion port;
- (b) drawing sufficient of a casting solution into an inner bore of the extrusion port;
- (c) delivering the coagulant (an aqueous solution containing biological material) through the inner bore to form a coextruded inner core;
- (d) terminating delivery of the coagulant, and
- (e) terminating delivery of the casting solution to achieve a smooth end to the capsule, so that the coaxial rod extends through the capsule and is continuous with

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the first end but not the second end.

The casting solution and coagulant are selected so that coagulation occurs as the solutions are extruded.

USE - The capsules are suitable for encapsulation of biologically active factors and are especially suitable for use as therapeutic implants (e.g. for the treatment of Parkinson's disease) and artificial organs capable of secreting biological factors (e.g. insulin and thymic factors). The extrusion of the casting solution may be continued to form a tether which allows the capsule to be located close to the target region while the end of remains easily accessible.

Full	Title	Citation Front	Review	Classification	Date	Reference		Claims	KMC	Draw, Desi
				,						
	7.	Document ID:	US 54	418154 A	***************************************	,				

# **Hit List**

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Search Results - Record(s) 1 through 5 of 5 returned.

☐ 1. Document ID: US 4181467 A

Using default format because multiple data bases are involved.

L4: Entry 1 of 5

File: USPT

Jan 1, 1980

US-PAT-NO: 4181467

DOCUMENT-IDENTIFIER: US 4181467 A

TITLE: Radially curved axial cross-sections of tips and sides of diffuser vanes

DATE-ISSUED: January 1, 1980

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Campbell; Kenneth

Ridgewood

NJ

US-CL-CURRENT: 415/207; 415/208.3

Full Title Citation Front Review Classification Date Reference Station State Claims KMC Draws Described De

L4: Entry 2 of 5

File: USPT

Jul 11, 1978

US-PAT-NO: 4099891

DOCUMENT-IDENTIFIER: US 4099891 A

\*\* See image for Certificate of Correction \*\*

TITLE: Sawtoothed diffuser, vaned, for centrifugal compressors

DATE-ISSUED: July 11, 1978

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Campbell; Kenneth

Ridgewood

NJ

US-CL-CURRENT: 415/207; 415/208.3

ABSTRACT:

This invention is proposed as an aerodynamically more efficient vaned diffuser for centrifugal compressors than heretofore achieved, while still respecting the usual diffuser requirement of a limited overall diameter. The invention is so to shape the early entering portion of the diffuser side-walls and the vanes as to achieve for the first time, isobars across the so-called throat which are highly oblique to the flow direction there, instead of heretofore always an isobar which is very nearly normal or normal across the passage at that throat. This is more understandably but still

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briefly explained in the two sections following, on Background, and Summary, of the Invention.

6 Claims, 5 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Front Review Classification Date Reference

Claims KMC Draw Desi

☐ 3. Document ID: US 3481866 A

L4: Entry 3 of 5

File: USPT

Dec 2, 1969

US-PAT-NO: 3481866

DOCUMENT-IDENTIFIER: US 3481866 A

TITLE: EXTRACTION OF LEAD FROM PETROLEUM PRODUCTS EMPLOYING AQUEOUS IODINE

MONOCHLORIDE

DATE-ISSUED: December 2, 1969

INVENTOR-INFORMATION:

NAME

CITY STATE ZIP CODE

COUNTRY

MOSS RONALD

CAMPBELL KENNETH GRIFFITHS SAMUEL T

US-CL-CURRENT: 208/251R; 208/88

Full Title Citation Front Review Classification Date Reference Claims KWC Draw. Desc

☐ 4. Document ID: GB 2149687 A

L4: Entry 4 of 5

File: EPAB

Jun 19, 1985

PUB-NO: GB002149687A

DOCUMENT-IDENTIFIER: GB 2149687 A

TITLE: Method for the regeneration of catalytic exhaust gas converters for internal

combustion and compositions for use therein

PUBN-DATE: June 19, 1985

INVENTOR-INFORMATION:

NAME

COUNTRY

GROVES, JOHN

CAMPBELL, KENNETH

US-CL-CURRENT: 502/35

INT-CL (IPC): B01J 23/96

EUR-CL (EPC): B01J023/96; B01D053/94

ABSTRACT:

Lead poisoned catalytic exhaust gas converters are regenerated by passing HCl and/or HBr vapour through the converter at elevated temperature. Regeneration can be effected with the converter still connected to the exhaust system of the vehicle simply by adding an organobromo and/or organochloro compound to the fuel, which is preferably an unleaded gasoline.

Full Title Citation Front Review Classification Date Reference Claims KWC Draw Description 5. Document ID: US 3481866 A

File: USOC

Dec 2, 1969

US-PAT-NO: 3481866

L4: Entry 5 of 5

DOCUMENT-IDENTIFIER: US 3481866 A

TITLE: EXTRACTION OF LEAD FROM PETROLEUM PRODUCTS EMPLOYING AQUEOUS IODINE

MONOCHLORIDE

DATE-ISSUED: December 2, 1969

US-CL-CURRENT: 208/251R; 208/88

## DOCUMENT TEXT:

Unieted'r6%tates Patent Office 394819866 3,481,866 EXTRACTION OF LEAD FROM PETROLELTM PRODUCTS EMPLOYING AQUEOUS IODINE MONOCHLORIDE Ronald Moss, Upton, Chester, and Kenneth Campbell iind Samuel T. Griffiths, Bletchley, England, assignors to The Associated OcteI Company Limited, London, England No Drawing. Filed Oct. 17, 1967, Ser. No. 675,774 Claims priority, apphcation Great Britain, Aug. 17, 1967, 37,984/67 Int. Cl. Clog 21106 U.S. Cl. 208-251 4 Claims ABSTRACT OF THE DISCLOSURE Lead alkyl containing petroleum products, particularly gasoline and catalytic reformer feedstocks, are freed from their lead content by treatment with aqueous iodine monochloride. This invention relates to the extraction of lead from hydrocarbon f@edstock, gasoline and other petroleum products. The addition of lead compounds, especially lead alkyls such as tetraethyl lead and tetramethyl lead, to gasoline and other petroleum products is common practice. For certain purposes it is necessary subsequently to extract the lead from the gasoline. For example it may be iiecessary to extract the lead if the gasoline is to be subjected to reprocessing, for example, in a catalytic reformer in which the gasoline may be used as a feedstock or feedstock supplement. In this case it is important that the lead be reduced to as low a level as possible, preferably to below 50 par- ts per thousand million, in order to mim'mise poisoning of the catalyst, which is usually platinum. , Known methods for the extraction of lead from petroleum pr(>ducts involve the extraction of the lead by treatment of the leaded product with hydrochloric or sulphuric acid. The former procedure forms the basis of the standard methods for the determination of lead in gasoline, IP 96/,64 and ASTM D526. Whilst these inethods are satisfactory for analytical purposes and small scale operations they are not suitable for application on a large scale. In accordance with the present invention a method of extracting lead from gasoline and other petroleum products has been found which, being quick and substantially 100% efficient, is capable of application on, a large scale. The invention is based on the discovery that lead alkyls in gasoline or other petroleum products will react quantitatively with iodine monochloride to form water soluble dialkyl lead halides. The method of the present invention therefore comprises treating the lead alkyl containing gasoline or other lead alkyl containing petroleum product with an aqueous solution of iodine monochloride, thoroughly mixing the inorganic phase with the organic phase, and separating the organic phase from the inorganic phase. By this method substantially complete- extraction of the lead from the organic phase into the inorganic phase is obtained leaving the gasoline or other petroleum product substantially free of lead. Since the reaction of the iodine

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monochloride with the lead alkyl is quantitative the amount of iodine monochloride can be stoichiometric in relation to the amount of lead alkyl present in the petroleum product. More usually, however, the amount of iodine monochloride used will be in excess of stoichiometric. T'he concentration of the iodine monochloride solution used in the method of the invention wiR, of course, vary Patented Dec. 2, 1969 2 th the volume of gasoline or petroleum product to treated. As a matter of convenience the solutions used will usually be in the range 0.1-2.0 molar. Where the petroleum product contains any significant amount of olefin higher amounts of iodine monochloride will be used because iodine monochloride reacts readily with an olefinic double bond. The extraction is performed quite conveniently at room temperature. 10 In order to demonstrate the extraction of lead alkyls from petroleum products in accordance with this inven- tion a number of test samples were made up by blending various proportions of virgin naphtha, isooctane andkerosine. The samples were made up to simulate petroleum 15 ranging from a typical catalytic reformer feedstock on the one hand to an aviation turbine fuel on the other. A known quantity of lead alkyl, either tetramethyl lead, tetraethyl lead or a mixed lead alkyl obtained by a rearrangement reaction of tetraethyl lead and tetramethyl 20 lead, was added to each sample. Various volumes of each sample were taken and shaken at room temperature in a separating funnel with 10 ml. portions of a 1.0 molar aqueous solution of iodine monochloride. After shaking for three minutes the inorganic 25 phase was separated and the organic phase washed three times with 10 ml. portions of water. The washings were added to the separated inorganic phase and the lead content of the collected inorganic phase was determined colorimetrically by the well known dithizonate procedure. The 30 results were as follows, the weight of lead extracted is the average of two determinations. Weight o f lead 3 5 Volume a lkyl r atio a dded Weight S aTnple sample: c alculated o f lead v olume, I 01 a s lead, e xtracted, ml. s olution mg. mg. S ample No.: I 5 0 6 :1 2 1 2 1 4 0 2 ----: --------- 5 0 5 :1 4 2 4 0 3 ------ 5 0 5 :1 6 3 6 2 4 ----- 5 0 5 :1 8 4 8 4 5 ----- 5 00 6 0:1 2 1 2 0 6 -----5 00 5 0:1 4 2 4 0 7 ------ 5 00 6 0:1 6 3 6 1 8 --------- 5 00 5 0:1 8 4 8 3 4 5 1 1 ,000 1 00:1 2 1 2 2 1 6 1 ,000 1 00:1 4 2 4 5 1 1 -------1 ,000 1 00:1 6 3 6 0 1 2 ------ 1 ,000 1 00:1 8 4 8 4 These results clearly demonstrate the substantially 50 complete extraction which is achieved by the method of the present invention. They also clearly demonstrate the efficiency of a single extraction which is maintained even with sample: extractant ratios -as high as 100: 1. Whilst the invention is particularly applicable to the 55 extraction of lead from catalytic reformer feedstocks, it may also be applied to the extraction of lead from a wide range of petroleum products ranging from crud6 oil to light petroleum fractions. We claim: 60 1. The process which comprises treating a petroleum product containing lead alkyl with an aqueous solution of iodine monochloride, thoroughly mixing the inorganic phase with the organic phase, and subsequently separating the two phases, thereby removing the lead from the 65 said petroleum product. 2. The process of claim 1, wherein the amount of iodine monochloride used to treat the lead alkyl-containing petroleum product is in excess of the stoichiometric amount required to react with the lead alkyl in the prod- 70 uct under treatment. 3. The process of claim I wherein the iodine

monochloride solution used is 0. 1-2.0 molar.

Full Title Citation Front Review Class	sification Date Reference	Claims KWIC Draw, Des
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Search Results - Record(s) 1 through 19 of 19 returned.

☐ 1. Document ID: US 20040088392 A1

Using default format because multiple data bases are involved.

L5: Entry 1 of 19

File: DWPI

May 6, 2004

DERWENT-ACC-NO: 2004-410223

DERWENT-WEEK: 200438

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TITLE: Simulation system simulates movement of entities in network after generating

travel plans for each entity using activities of each entity

INVENTOR: BAGGERLY, K A; BARRETT, C L; BECKMAN, R J; BERKBIGLER, K P; BUSH, B W;

CAMPBELL, K ; ESSER, J ; EUBANK, S G ; JACOB, R R ; KONJEVOD, G ; MARATHE, M V ;

MCKAY, M D ; NAGEL, K ; SMITH, J P ; SPECKMAN, P L ; STRETZ, P E

PRIORITY-DATA: 2002US-0100501 (March 18, 2002)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 20040088392 A1

May 6, 2004

070

G06F015/173

INT-CL (IPC):  $\underline{606} + \underline{15/173}$ 

Full Title Citation Front Review Classification Date Reference

Cla KMC Draw Des

Document ID: EP 1456374 A2, WO 2003046141 A2, US 20030232430 A1, AU 2002360424 A1

L5: Entry 2 of 19

File: DWPI

Sep 15, 2004

DERWENT-ACC-NO: 2003-513640

DERWENT-WEEK: 200460

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TITLE: Producing a diploid human pronucleus for generating stem cells from which autologous, isogenic cells for transplantation therapy are derived by exposing the nucleus of a differentiated human cell to the cytoplasm of an oocyte

INVENTOR: CAMPBELL, K; CIBELLI, J; WEST, M

PRIORITY-DATA: 2001US-332510P (November 26, 2001), 2002US-0304020 (November 26, 2002)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 EP 1456374 A2
 September 15, 2004
 E
 000
 C12N015/00

WO 2003046141 A2 June 5, 2003 E 063 C12N000/00

US 20030232430 A1 AU 2002360424 A1 December 18, 2003

June 10, 2003

C12N005/08

000 C12N000/00

000

INT-CL (IPC): C12 N 0/00; C12 N 5/08; C12 N 15/00

ABSTRACTED-PUB-NO: WO2003046141A

BASIC-ABSTRACT:

NOVELTY - Producing a diploid human pronucleus comprising exposing the nucleus of a differentiated human cell to the cytoplasm of an oocyte, is new.

USE - The method is useful for generating stem cells from which autologous, isogenic cells for transplantation therapy are derived. The method is useful for identifying and analyzing the molecular mechanisms of epigenetic imprinting and the genetic regulation of embryogenesis and development.

Full Title Citation Front	Review Classification	Date Reference		Cla	KMMC   Draw. Desc

# ☐ 3. Document ID: AU 2002331772 A1, US 20030046626 A1, WO 2003021445 A1, EP 1423790 A1

L5: Entry 3 of 19

File: DWPI

Mar 18, 2003

DERWENT-ACC-NO: 2003-429681

DERWENT-WEEK: 200452

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TITLE: Test tool providing method for generating test scripts involves providing test codes to each acceptable alternate behavior when providing test code to non-deterministic behavior

INVENTOR: CAMPBELL, K; DAVID, N W; HAND, W C; NOORDA, E; SAVAGE, P; SEELEY, A; TRUMPLER, M

PRIORITY-DATA: 2001US-0943640 (August 30, 2001)

### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 2002331772 A1	March 18, 2003		000	G06F011/36
US 20030046626 A1	March 6, 2003		005	G06F011/00
WO 2003021445 A1	March 13, 2003	E	000	G06F011/36
EP 1423790 A1	June 2, 2004	E	000	G06F011/36

INT-CL (IPC):  $\underline{G06} \ \underline{F} \ \underline{9/44}; \ \underline{G06} \ \underline{F} \ \underline{11/00}; \ \underline{G06} \ \underline{F} \ \underline{11/36}; \ \underline{G06} \ \underline{F} \ \underline{17/50}; \ \underline{H04} \ \underline{M} \ \underline{3/24}$ 

ABSTRACTED-PUB-NO: US20030046626A

BASIC-ABSTRACT:

NOVELTY - The method entails providing test codes for testing deterministic and non-deterministic behaviors within an application. A test code is provided to the non-deterministic behavior by providing test codes for each of the acceptable alternate behaviors associated with the non-deterministic behavior.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a computer program product.

USE - For generating test scripts to test application in CIT (computer integrated

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telephony) systems.

ADVANTAGE - Permits graphical programming of tests for application while taking nondeterministic behavior of application into account. Simplifies usage.

DESCRIPTION OF DRAWING(S) - The figure is a screen shot showing icons and connectors used to test for deterministic and non-deterministic behavior in an application.

Full Title Citation Front Review Classification Date Reference Cla KMIC Draw Description

4. Document ID: US 6420969 B1

L5: Entry 4 of 19

File: DWPI

Jul 16, 2002

DERWENT-ACC-NO: 2002-654663

DERWENT-WEEK: 200270

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TITLE: Activation state determining system for central alarm system, includes electrical relay which prevents or allows operation of arming control, when ON or OFF state of appliance switch is detected respectively

INVENTOR: CAMPBELL, K

PRIORITY-DATA: 2000US-0568574 (May 10, 2000)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 6420969 B1

July 16, 2002

007

G08B029/00

INT-CL (IPC):  $\underline{G08} \ \underline{B} \ \underline{21/00}; \ \underline{G08} \ \underline{B} \ \underline{29/00}$ 

ABSTRACTED-PUB-NO: US 6420969B

BASIC-ABSTRACT:

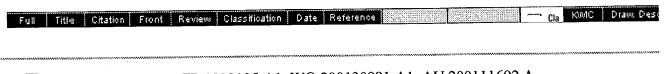
NOVELTY - An electrical relay prevents or allows the operation of the arming control (18) of an intrusion alarm, when ON or OFF state of an appliance switch is detected respectively.

USE - For central alarm system.

ADVANTAGE - Diminishes the possibility of unsafe condition due to ON or unattended state of appliance, by controlling operation of arming control based on state of appliance switch.

DESCRIPTION OF DRAWING(S) - The figure shows the interaction between appliance and central alarm system.

Arming control 18



Document ID: EP 1228195 A1, WO 200130981 A1, AU 200111692 A

L5: Entry 5 of 19

File: DWPI

Aug 7, 2002

DERWENT-ACC-NO: 2001-335700

DERWENT-WEEK: 200259

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TITLE: New in vitro adhesion culture of glial fibrillary acidic protein immunoreactive (GFAP positive) cells useful for proliferating and differentiating GFAP positive nestin positive cells for transplantation to patients with Parkinson's disease

INVENTOR: CAMPBELL, K ; ERIKSSON, C ; FAGERSTROM, C ; WAHLBERG, L ; WICTORIN, K

PRIORITY-DATA: 2000US-0161316 (October 24, 2000), 1999US-161316P (October 25, 1999)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1228195 A1	August 7, 2002	E	000	C12N005/06
WO 200130981 A1	May 3, 2001	E	064	C12N005/06
AU 200111692 A	May 8, 2001		000	C12N005/06

INT-CL (IPC): A61 K 35/30; A61 K 48/00; C12 N 5/06; C12 N 5/08; C12 N 5/10; C12 N 5/16;

# **Hit List**

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# Search Results - Record(s) 1 through 27 of 27 returned.

1. Document ID: US 20040028093 A1

Using default format because multiple data bases are involved.

L11: Entry 1 of 27

File: DWPI

Feb 12, 2004

DERWENT-ACC-NO: 2004-237530

DERWENT-WEEK: 200422

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TITLE: Photonic device includes doped conductive path within substrate for establishing electrical connection between metallic contact pad and peripheral

metallic frame

INVENTOR: ERIKSSON, C; FRODE, J; ZETTERLUND, E

PRIORITY-DATA: 2002GB-0010411 (May 8, 2002)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 20040028093 A1

February 12, 2004

004

H01S003/13

INT-CL (IPC):  $\underline{\text{H01}} \ \underline{\text{S}} \ \underline{3/00}; \ \underline{\text{H01}} \ \underline{\text{S}} \ \underline{3/04}; \ \underline{\text{H01}} \ \underline{\text{S}} \ \underline{3/13}$ 

Full Title Citation Front Review Classification Date Reference

Document ID: AU 2003281507 A1, WO 2004009184 A1, SE 200202275 A, SE 523026 C2

L11: Entry 2 of 27

File: DWPI

Feb 9, 2004

10/27/04

DERWENT-ACC-NO: 2004-123295

DERWENT-WEEK: 200450

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TITLE: Chest musculature training machine, has supporting plates indirectly-articulatedly connected to carrier and configured to turn between starting position at acute angle to vertical folded up position

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 2002SE-0002275 (July 18, 2002)

PATENT-FAMILY:

PAGES MAIN-IPC PUB-DATE LANGUAGE PUB-NO A63B023/08 000 February 9, 2004 AU 2003281507 A1 A63B023/08 014 Ε WO 2004009184 A1 January 29, 2004 A63B023/02 000 January 19, 2004 SE 200202275 A

INT-CL (IPC): A63 B 23/02; A63 B 23/08; A63 B 23/12

ABSTRACTED-PUB-NO: WO2004009184A

BASIC-ABSTRACT:

NOVELTY - The machine has supporting plates (8) located on a level above a seat (3). Users forearms are pressable against the plates mounted on a carrier (9) on a turnable arm (10). The arms are moved against the effect of a counter load device. The plates are indirectly-articulatedly connected to the carrier and configured to turn between a starting position at an acute angle to a vertical, folded up position.

USE - Used for training chest musculature.

ADVANTAGE - The machine initiates the movement of the supporting plates from the outer end positions to the more central working portions without harmful breaks or muscles strains arising in the shoulder portion of the user. The machine can be entered and left by user in a simple and smooth way. The machine can be manufactured in a structurally simple way, while reducing the total building height of the machine.

 ${\tt DESCRIPTION}$  OF  ${\tt DRAWING(S)}$  — The drawing shows a simplified view of a training machine.

Stand 1

Seat 3

Supporting plates 8

Carrier 9

Turnable arm 10

Ī	Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KWAC	Draw, Desc
*********	***************************************	**********	·····			······		······	······			***************************************	
		3.	Docume	ent ID:	WO 2	.003002338	3 A1,	SE 20010	2306 A, S	SE 520783 C	2, EP 1	40451	4 A1,
	US 2	20040	0142107	A1, A	U 2002	314668 A	l						

File: DWPI

DERWENT-ACC-NO: -2003-247914

L11: Entry 3 of 27

DERWENT-WEEK: 200461

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TITLE: Manufacture of decorative surface element e.g. floor boards, involves orienting fiber closest to upper surface in predetermined pattern, and applying pigmentation and protective lacquer on upper surface

INVENTOR: ERIKSSON, C; LARSSON, R

PRIORITY-DATA: 2001SE-0002306 (June 28, 2001)

PATENT-FAMILY:

PUB-NO PUB-DATE LANGUAGE PAGES MAIN-IPC WO 2003002338 A1 January 9, 2003 E 011 B32B005/12

Jan 9, 2003

SE 200102306 A	December 29, 2002		000	B44C005/04
SE 520783 C2	August 26, 2003		000	B44C005/04
EP 1404514 A1	April 7, 2004	E	000	B32B005/12
US 20040142107 A1	July 22, 2004		000	B05D001/36
AU 2002314668 A1	March 3, 2003		000	B32B005/12

INT-CL (IPC):  $\underline{B05}$   $\underline{D}$   $\underline{1/36}$ ;  $\underline{B05}$   $\underline{D}$   $\underline{5/00}$ ;  $\underline{B32}$   $\underline{B}$   $\underline{5/12}$ ;  $\underline{B44}$   $\underline{C}$   $\underline{5/04}$ 

ABSTRACTED-PUB-NO: WO2003002338A

BASIC-ABSTRACT:

NOVELTY - A decorative surface element is manufactured by orienting the fiber closest to upper surface in predetermined pattern, applying pigmentation on the upper surface, and applying protective lacquer on the upper surface.

USE - For manufacturing decorative surface element e.g. floor boards, wall panels and ceiling panels.

ADVANTAGE - The process provides a decorative surface element having a decor appearance that changes with the angle of view.

Full   Title   Citation   Front   Review   Classific	Claims   KWC   Draw Desc
☐ 4. Document ID: US 2003000	Jan 2, 2003

DERWENT-ACC-NO: 2003-185920

DERWENT-WEEK: 200319

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TITLE: Integrated photodetector for wavelength division multiplexing application, has bandgap filter arrangement that includes progressively varying bandgap in upstream direction across filter layers

INVENTOR: ERIKSSON, C ; JOENGREN, P ; JONGREN, P

PRIORITY-DATA: 2001GB-0013965 (June 8, 2001), 2001GB-0013964 (June 8, 2001)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 US 20030001167 A1
 January 2, 2003
 000
 H01L033/00

 EP 1265296 A1
 December 11, 2002
 E
 012
 H01L031/0232

INT-CL (IPC):  $\underline{\text{H01}}$   $\underline{\text{L}}$   $\underline{27/146}$ ;  $\underline{\text{H01}}$   $\underline{\text{L}}$   $\underline{31/0216}$ ;  $\underline{\text{H01}}$   $\underline{\text{L}}$   $\underline{31/0232}$ ;  $\underline{\text{H01}}$   $\underline{\text{L}}$   $\underline{33/00}$ 

ABSTRACTED-PUB-NO: EP 1265296A

BASIC-ABSTRACT:

NOVELTY - A bandgap filter arrangement comprising a stack of filter layers (121 - 12n) provided on the upstream of a detector which generates output signal in response to the incident light. The arrangement has progressively varying bandgap in the upstream direction across the filter layers.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for light detection method.

USE - For wavelength division multiplexing applications for broadband communication.

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.12&ref=11&dbname=PGPB,USPT,U... 10/27/04

ADVANTAGE - The bandgap filter arrangement effectively removes the short wavelength components and attenuates low photonic power.

DESCRIPTION OF DRAWING(S) - The figure shows a schematic view of the integrated photodetector.

Filter layers 121 - 12n

Full Title Citation Front Review Classification Date Reference Claims KWIC Draw Description 5. Document ID: SE 200101505 A
L11: Entry 5 of 27 File: DWPI Oct 29, 2002

DERWENT-ACC-NO: 2003-118952

DERWENT-WEEK: 200311

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TITLE: Building component comprises two flat parallel plates, between which is stiffening and insulating layer comprising parallel cells with tubular walls

INVENTOR: BERGSTROEM, D; ERIKSSON, C; JONSSON, T; LUNDQUIST, H

PRIORITY-DATA: 2001SE-0001505 (April 28, 2001)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 SE 200101505 A
 October 29, 2002
 001
 E04C002/36

INT-CL (IPC): B32 B 3/12; E04 C 2/36

ABSTRACTED-PUB-NO: SE 200101505A

BASIC-ABSTRACT:

NOVELTY - The building component comprises two flat parallel plates, between which is a stiffening and insulating layer comprising parallel cells with tubular walls extending between the two plates. The surface sections of the two plates form end walls, which contain air or another gas with as low a pressure as pumping technique can produce. The spaces formed by the cell tubular walls are separated from each other in an air-tight manner. They are also thus separated from the atmosphere.

USE - As a building insulating component.

ADVANTAGE - The structure of the component is such that the stiffening and insulating layer between the two basic plates of the component comprises cells which are separated from each other in an air-tight manner. They are also isolated from the atmosphere.

DESCRIPTION OF DRAWING(S) - The figure is an exploded view of the constituents of the building component.

☐ 6. Document ID: WO 200225620 A1, SE 200003340 A, SE 517181 C2, AU 200188174 A, US 20040096809 A1

L11: Entry 6 of 27 File: DWPI Mar 28, 2002

DERWENT-ACC-NO: 2002-315760

DERWENT-WEEK: 200446

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TITLE: Reading aid for use in, e.g. schools or office environments, comprises tongue

that is integral with ruler and grooving line extending to be in longitudinal

direction of the ruler

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 2000SE-0003340 (September 19, 2000)

#### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200225620 A1	March 28, 2002	E	013	G09B017/02
SE 200003340 A	March 20, 2002		000	•
SE 517181 C2	April 23, 2002		000	•
AU 200188174 A	April 2, 2002		000	
US 20040096809 A1	May 20, 2004		000	G09B021/00

INT-CL (IPC):  $\underline{G09} \ \underline{B} \ \underline{17/02}; \ \underline{G09} \ \underline{B} \ \underline{21/00}$ 

ABSTRACTED-PUB-NO: WO 200225620A

BASIC-ABSTRACT:

NOVELTY - A reading aid in a ruler shape comprises a tongue (3) that is integral with the ruler (1) and a grooving line (7) placed between the ruler and the tongue. The grooving line extends transverse to be in a longitudinal direction of the ruler.

USE - The reading aid is for use in schools or office environments. It can also be used in connections with letters, figures or signs; or to aim stitches, e.g. in connection with embroidery.

ADVANTAGE - The inventive reading aid is simple and functions in a user-friendly way. It can be manufactured at a comparatively low cost and from a material that may be recycled.

DESCRIPTION OF DRAWING(S) - The figure shows the reading aid mounted on a page of a book.

Ruler 1

Tongue 3

Grooving line 7

Holes 9

											,
Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	KWIC	Draw, Desc
		,									-

7. Document ID: US 6739607 B2, WO 200194190 A1, SE 200002104 A, SE 516438 C2, AU 200164462 A, NO 200200562 A, EP 1198381 A1, US 20020113395 A1

L11: Entry 7 of 27

File: DWPI

May 25, 2004

DERWENT-ACC-NO: 2002-062605

DERWENT-WEEK: 200435

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TITLE: Device for damping pivotal movements of wheel-supporting pendular arm of motor vehicle has movable piston between spring unit and pressure plates, and restrictor allowing hydraulic pressure medium to flow from one side of piston to other

INVENTOR: BODIN, A; ERIKSSON, C

PRIORITY-DATA: 2000SE-0002104 (June 6, 2000)

#### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6739607 B2	May 25, 2004		000	B62D055/104
WO 200194190 A1	December 13, 2001	E	019	B62D055/108
SE 200002104 A	December 7, 2001		000	B62D055/108
SE 516438 C2	January 15, 2002		000	B62D055/108
AU 200164462 A	December 17, 2001		000	B62D055/108
NO 200200562 A	March 25, 2002		000	B62D000/00
EP 1198381 A1	April 24, 2002 -	E	000	B62D055/108
US 20020113395 A1	August 22, 2002		000	B60G011/26

INT-CL (IPC): <u>B60 G 11/26</u>; <u>B60 G 13/04</u>; <u>B62 D 0/00</u>; <u>B62 D 55/104</u>; <u>B62 D 55/108</u>; <u>F16 D</u> 3/14

ABSTRACTED-PUB-NO: US20020113395A

BASIC-ABSTRACT:

NOVELTY - The damper has a first pressure plate (28) torsionally fixed but axially movable on the swing axle of a pendular arm. A second pressure plate (30) is movable in the housing (16). A compression spring unit (42,44) exerts a compressive force on the pressure and disk plates. A movable piston (46) is arranged between the spring unit and the pressure plates. A restrictor element (50) allows hydraulic pressure medium to flow from one side of the piston to the other.

USE - For damping of tracked vehicles.

ADVANTAGE - Permits both position dependent and speed dependent damping of pendular arms.

DESCRIPTION OF DRAWING(S) - The drawing shows an enlarged cross sectional view of the damper.

Housing 16

Pressure plates 28,30

Compression spring unit 42,44

Piston 46

Restrictor element 50 ABSTRACTED-PUB-NO:

WO 200194190A EQUIVALENT-ABSTRACTS:

NOVELTY - The damper has a first pressure plate (28) torsionally fixed but axially movable on the swing axle of a pendular arm. A second pressure plate (30) is movable

in the housing (16). A compression spring unit (42,44) exerts a compressive force on the pressure and disk plates. A movable piston (46) is arranged between the spring unit and the pressure plates. A restrictor element (50) allows hydraulic pressure medium to flow from one side of the piston to the other.

USE - For damping of tracked vehicles.

ADVANTAGE - Permits both position dependent and speed dependent damping of pendular arms.

DESCRIPTION OF DRAWING(S) - The drawing shows an enlarged cross sectional view of the damper.

Housing 16

Pressure plates 28,30

Compression spring unit 42,44

Piston 46

Restrictor element 50

Full	Title	Citation	Front	Review	Classification	Date	Reference			0	laims	KOMC	Drawi Desi
	·····					,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			·····	······································			
	8.	Docume	nt ID:	SE 200	0002406 A	, US	20020022	2556 A1, S	SE 5158	364 C2	EP 1	16682	27 A2
L11:	Enti	ry 8 of 2	27				File:	DWPI			Oct	22,	2001

DERWENT-ACC-NO: 2002-016809

DERWENT-WEEK: 200221

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TITLE: Exercise machine for back muscles, has back rest separate from seat and mounted on swing arm

INVENTOR: ERIKSSON, B; ERIKSSON, C

PRIORITY-DATA: 2000SE-0002406 (June 26, 2000)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
SE 200002406 A	October 22, 2001		001	A63B023/08
US 20020022556 A1	February 21, 2002		000	A63B021/00
SE 515864 C2	October 22, 2001		000	A63B023/08
EP 1166827 A2	January 2, 2002	E	000	A63B023/02

INT-CL (IPC):  $\underline{A63}$   $\underline{B}$   $\underline{21/00}$ ;  $\underline{A63}$   $\underline{B}$   $\underline{23/02}$ ;  $\underline{A63}$   $\underline{B}$   $\underline{23/08}$ 

ABSTRACTED-PUB-NO: SE 200002406A

BASIC-ABSTRACT:

NOVELTY - The machine has a seat (2) mounted on a frame, a back rest (17) positioned above the seat, and a main arm (12) which is pivotable about a main link (13) to oppose the force exerted by a counter-load device (3). The back rest is separate from the seat and joined via swing arm (19) to a part of the main arm above the main link, the swing arm being joined to the main arm via a sec. link (20). The back rest is mounted on a cross-beam (18) extending at an angle to the swing arm. The back rest

can be moved between front and rear end positions via an orbital path in which it is free to move between different radial positions relative to the main joint, depending on back movements of the person using the machine.

USE - None given.

ADVANTAGE - None given.

DESCRIPTION OF DRAWING(S) - Figure 1 shows a side view of the exercise machine.

Seat 2

Counter-load device 3

Main arm 12

Main link 13

Back rest 17

Cross beam 18

Swing arm 19

Sec. link 20

ABSTRACTED-PUB-NO:

US20020022556A EQUIVALENT-ABSTRACTS:

NOVELTY - The machine has a seat (2) mounted on a frame, a back rest (17) positioned above the seat, and a main arm (12) which is pivotable about a main link (13) to oppose the force exerted by a counter-load device (3). The back rest is separate from the seat and joined via swing arm (19) to a part of the main arm above the main link, the swing arm being joined to the main arm via a sec. link (20). The back rest is mounted on a cross-beam (18) extending at an angle to the swing arm. The back rest can be moved between front and rear end positions via an orbital path in which it is free to move between different radial positions relative to the main joint, depending on back movements of the person using the machine.

USE - None given.

ADVANTAGE - None given.

DESCRIPTION OF DRAWING(S) - Figure 1 shows a side view of the exercise machine.

Seat 2

Counter-load device 3

Main arm 12

Main link 13

Back rest 17

Cross beam 18

Swing arm 19

Sec. link 20

Full Title Citation Front Review Classification Date Reference (1997) 1997 | 1997 | Claims KMC Draw Desc

☐ 9. Document ID: SE 9904042 A

L11: Entry 9 of 27

File: DWPI

May 9, 2001

DERWENT-ACC-NO: 2001-439911

DERWENT-WEEK: 200147

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TITLE: Lock cylinder has cylindrical wall, inside which are several rotatable lock plates, cylinder containing device for transmitting rotary movement in cylinder to part of lock device

INVENTOR: ANDREE, R; ERIKSSON, C; HELGESSON, M

PRIORITY-DATA: 1999SE-0004042 (November 8, 1999)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

SE 9904042 A

May 9, 2001

001

E05B017/04

INT-CL (IPC): E05 B 17/04; E05 B 17/20; E05 B 21/06

ABSTRACTED-PUB-NO: SE 9904042A

BASIC-ABSTRACT:

NOVELTY - The lock cylinder (56) has a cylindrical wall (57), inside which are several rotatable lock plates (59). The cylinder contains a device (81) arranged on the cover surface for transmitting a rotary movement in the cylinder to a part in the lock device.

USE - As a lock cylinder forming part of a lock arrangement.

Full	Title Cit.	tion Front	Review	Classification	Date	Reference		Claims	KMC	Drawl Desk
·····							······	 ••••••		
	10. De	ocument II	D: <b>SE</b> 9	904041 A						
L11:	Entry 1	0 of 27				File	: DWPI	Ма	у 9,	2001

DERWENT-ACC-NO: 2001-439910

DERWENT-WEEK: 200147

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TITLE: Lock cylinder comprises cylindrical wall, end wall at one end and lock plates rotatably fitted inside cylindrical wall, end wall having aperture for receiving lock device

INVENTOR: ANDREE, R; ERIKSSON, C; HELGESSON, M

PRIORITY-DATA: 1999SE-0004041 (November 8, 1999)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

SE 9904041 A

May 9, 2001

001

E05B017/20

INT-CL (IPC):  $\underline{E05} \ \underline{B} \ \underline{17/20}$ ;  $\underline{E05} \ \underline{B} \ \underline{21/06}$ 

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.12&ref=11&dbname=PGPB,USPT,U...

ABSTRACTED-PUB-NO: SE 9904041A BASIC-ABSTRACT:

NOVELTY - The lock cylinder comprises a cylindrical wall (57), end wall (58) at one end of cylinder (56) and number of lock plates (59) rotatably fitted inside the cylindrical wall. The end wall has an aperture (82) for receiving a lock device. The aperture extends forwards to one of the lock plates so that the lock part, via the aperture, can locate against the lock plate.

USE - As a lock cylinder with a lock device.

DESCRIPTION OF DRAWING(S) - The figure illustrates a perspective view of the lock cylinder.

lock cylinder 56

cylindrical wall 57

end wall 58

lock plates 59

aperture 82

Full   T		lassification Date Reference	
		28195 A1, WO 200130981 A1, AU 2001	
L11: E1	ntry 11 of 27	File: DWPI	Aug 7, 2002

DERWENT-ACC-NO: 2001-335700

DERWENT-WEEK: 200259

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TITLE: New in vitro adhesion culture of glial fibrillary acidic protein immunoreactive (GFAP positive) cells useful for proliferating and differentiating GFAP positive nestin positive cells for transplantation to patients with Parkinson's disease

INVENTOR: CAMPBELL, K; ERIKSSON, C; FAGERSTROM, C; WAHLBERG, L; WICTORIN, K

PRIORITY-DATA: 2000US-0161316 (October 24, 2000), 1999US-161316P (October 25, 1999)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1228195 A1	August 7, 2002	Ε.	000 .	C12N005/06
WO 200130981 A1	May 3, 2001	E	064	C12N005/06
AU 200111692 A	May 8, 2001		000	C12N005/06

INT-CL (IPC): A61 K 35/30; A61 K 48/00; C12 N 5/06; C12 N 5/08; C12 N 5/10; C12 N 5/16; G01 N 33/48

ABSTRACTED-PUB-NO: WO 200130981A

BASIC-ABSTRACT:

NOVELTY - An in vitro adhesion cell culture of glial fibrillary acidic protein immunoreactive (GFAP+) cells, is new.

DETAILED DESCRIPTION - An in vitro adhesion cell culture GFAP+ cells, where:

- (a) one or more cells in the culture have the capacity to differentiate into neurones;
- (b) the cell culture divides in a culture medium containing serum (S) and at least one proliferation-inducing growth factor (PGF), and
- (c) one or more cells (I) in the culture have the capacity to differentiate into neurons, upon withdrawal of both (S) and PGF.

INDEPENDENT CLAIMS are also included for the following:

- (1) an in vitro cell culture (I) consisting essentially of a culture medium containing (S) and PGF, and cells derived from the central nervous system of a mammal, where the cells in the culture are GFAP+, capable of proliferating in a culture medium containing (S) and PGF, and capable of differentiating into neurons in the absence of both the (S) and PGF from the culture medium;
- (2) producing (P1) a neuronal cell in vitro, by obtaining neural tissue from a mammal, the neural tissue containing at least one GFAP+ cell capable of producing progeny that is a GFAP+ cell, dissociating the neural tissue to obtain\_a cell suspension comprising the GFAP+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate GFAP+ cell and produce a GFAP+ cell progeny, and differentiating the cell progeny in a second culture medium that is substantially free of both the (S) and PGF;
- (3) producing (P2) a non-neuronal cell in vitro, by P1, and differentiating the cell progeny in a second culture medium that is substantially free of (S);
- (4) producing (P3) a genetically modified GFAP+ cell, by P1, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (5) producing (P4) a genetically modified differentiated neural cell culture, by P1, and differentiating the cell progeny to contain at least 10% neurons in a second culture medium that is substantially free of both the (S) and PGF, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (6) producing (P5) a genetically modified non-neuronal cell culture, by P1, and differentiating the cell progeny to contain at least 10% glia in a second culture medium that is substantially free of (S), where the glia are GFAP+ and vimentin positive, and genetically modifying the non-neuronal cell;
- (7) transplanting GFAP+ nestin+ cell progeny to a host, by obtaining neural tissue from a mammal, the neural tissue containing at least one GFAP+ nestin+ cell capable of producing progeny that are capable of differentiating into neurons and glia, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ nestin+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate the GFAP+ nestin+ cell and produce GFAP+ nestin+ cell progeny, and transplanting the GFAP+ nestin+ cell progeny to the host;
- (8) determining the effect of at least one biological agent on a GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell progeny by the above said method, contacting the proliferated GFAP+ nestin+ cell with the biological agent, and determining the effect of biological agent on GFAP+ nestin+ cells;
- (9) determining the effect of at least one biological agent on the differentiation of GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said method, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate in a second culture medium in the presence of biological agent, and determining the effects of the biological agent on the differentiation of the GFAP+ nestin+ cells;

- (10) determining the effect of at least one biological agent on the differentiated GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said process, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate into neurons or glia, contacting the differentiated neural cells with the biological agent, and determining the effects of the biological agent on the differentiated neural cells;
- (11) a cDNA library prepared from (I); and
- (12) a cell population consisting essentially of isolated GFAP+ nestin+ cells.

ACTIVITY - Immunosuppressive; antiparkinsonian.

No supporting biological data given.

MECHANISM OF ACTION - None given.

USE - The culture method is useful for proliferating and differentiating GFAP+ nestin+ cells (claimed). The cultured cells are useful for transplantation procedures, particularly to patients suffering from Parkinsonian's disease.

Full Title Citation Front Review	Classification Date	Reference	Claims KMC Draw Desc
		١	
☐ 12. Document ID: US 6	6694857 B2, SE	200000535 A, SE 51	4605 C2, WO 200161266 A1,
AU 200134296 A, EP 1255957			
AU 200134290 A, El 1233937	A1, 05 200300	10100 111	
L11: Entry 12 of 27		File: DWPI	Feb 24, 2004

DERWENT-ACC-NO: 2001-233595

DERWENT-WEEK: 200415

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TITLE: Unloading device for removing shells from magazine, has two grabs for initial

and continued movement of shells

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 2000SE-0000535 (February 18, 2000)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6694857 B2	February 24, 2004		000	F41A009/43
SE 200000535 A	March 19, 2001		001	F41A009/00
SE 514605 C2	March 19, 2001		000	
WO 200161266 A1	August 23, 2001	E	000	F41A009/00
AU 200134296 A	August 27, 2001		000	F41A009/00
EP 1255957 A1	November 13, 2002	E	000	F41A009/00
US 20030010188 A1	January 16, 2003		000	F41A009/00

INT-CL (IPC):  $\underline{F41} \ \underline{A} \ \underline{9/00}$ ;  $\underline{F41} \ \underline{A} \ \underline{9/38}$ ;  $\underline{F41} \ \underline{A} \ \underline{9/43}$ ;  $\underline{F41} \ \underline{A} \ \underline{9/61}$ 

ABSTRACTED-PUB-NO: SE 200000535A

BASIC-ABSTRACT:

NOVELTY - The unloading device has a first grab for the main initial linear movement of a shell (G) from the magazine, and a second grab (56) for further movement of the shell into a removed position. As the second grab moves the shell into the end

position, the first grab can return to its starting position.

USE - None given.

ADVANTAGE - None given.

DESCRIPTION OF DRAWING(S) - Figures 8b and 8c show the shell unloading device.

Grab 56

Shell G 8b, 8c/3

Full Title Citation Front Review Classit	fication Date Reference	Claims KWC Draw Desi
☐ 13. Document ID: US 66624 A, EP 1127241 A1, AU 764505 B	84 B1, WO 200031491 A1, AU 20	00015918 A, NO 200102241
L11: Entry 13 of 27	File: DWPI	Dec 16, 2003

DERWENT-ACC-NO: 2000-400167

DERWENT-WEEK: 200382

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TITLE: Locking unit for a weapon, comprises a locking unit placed within the breech

block of the weapon to disable it from use

INVENTOR: ANDREE, R; ERIKSSON, C; HELGESSON, M

PRIORITY-DATA: 1998SE-0003857 (November 8, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6662484 B1	December 16, 2003		000	F41A017/00
WO 200031491 A1	June 2, 2000	E	053	F41A017/44
AU 200015918 A	June 13, 2000		000	F41A017/44
NO 200102241 A	May 7, 2001		000	F41A000/00
EP 1127241 A1	August 29, 2001	E	000	F41A017/44
AU 764505 B	August 21, 2003		000	F41A017/44
A0 701300 B				

INT-CL (IPC):  $\underline{E05}$   $\underline{B}$   $\underline{9/08}$ ;  $\underline{E05}$   $\underline{B}$   $\underline{17/20}$ ;  $\underline{E05}$   $\underline{B}$   $\underline{19/00}$ ;  $\underline{E05}$   $\underline{B}$   $\underline{37/00}$ ;  $\underline{E05}$   $\underline{B}$   $\underline{73/00}$ ;  $\underline{F41}$   $\underline{A}$ 0/00; <u>F41</u> <u>A</u> <u>17/00</u>; <u>F41</u> <u>A</u> <u>17/44</u>

ABSTRACTED-PUB-NO: WO 200031491A BASIC-ABSTRACT:

NOVELTY - The locking unit comprises a key unit (2) to which is attached a lock body (5). The lock body comprises a locking element (3) which has a number of tangs located at its end. Expansion of the tangs causes the lock unit to become wedged within the breech block of the weapon.

USE - Locking unit for a weapon particular for and assault rifle such as the type G3 manufactured by Heckler and Koch.

ADVANTAGE - The unit provides a non destructive means of disabling a weapon.

DESCRIPTION OF DRAWING(S) - The figure shows a perspective view of the locking unit

Key unit 2

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.12&ref=11&dbname=PGPB,USPT,U...

Full Title Citation Front Review Classification Date Reference

☐ 14. Document ID: SE 9803717 A, SE 512974 C2

L11: Entry 14 of 27

File: DWPI

May 1, 2000

DERWENT-ACC-NO: 2000-440536

DERWENT-WEEK: 200038

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TITLE: Transferring molten metal from smelt bath to e.g. press casting machine with scoop, using a slag rake on the scoop to prevent slag from entering via the scoop slit

INVENTOR: DAECKER, C; DAECKER, M U ; EDSTROEM, K ; ERIKSSON, C

PRIORITY-DATA: 1998SE-0003717 (October 30, 1998)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 SE 9803717 A
 May 1, 2000
 010
 B22D039/00

 SE 512974 C2
 June 13, 2000
 000
 B22D039/00

INT-CL (IPC): B22 D 39/00; B22 D 41/04

ABSTRACTED-PUB-NO: SE 9803717A

BASIC-ABSTRACT:

NOVELTY - The scoop (2) is swept horizontally across the bath surface (15) just before filling, so that the slag rake (11) on the scoop forms a slag-free area of the bath (9). DETAILED DESCRIPTION - A method for removing molten metal (8) from a smelt bath and supplying it to e.g. a press casting machine uses a scoop which is filled with molten metal by lowering it into the bath so that the metal flows in via a slit (7), after which the scoop is lifted out of the path and manoeuvered into a discharge location. Immediately prior to filling, the scoop is subjected to an at least partly horizontal sweeping movement, so that a slag rake protruding from the scoop in a direction at right angles to its travelling direction is located just beneath the bath surface and ensures essentially slag-free molten metal enters via the slit from the clean bath area (16). An INDEPENDENT CLAIM is also included for the smelt removal device used.

USE - For fully or partly automatic filling of molten metal, especially aluminium or alloys thereof, into e.g. press casting machines.

ADVANTAGE - Slag is prevented from being removed from the bath. DESCRIPTION OF DRAWING(S) - Figure 6 shows an overhead view of the smelt removal device. (1) Smelt removal device; (2) Scoop; (3) Spout; (4) Rear wall; (5) Base; (6) Sloping side walls; (7) Slit; (8) Smelt; (9) Smelt bath; (11) Slag rake; (12) Manoeuvering arm; (15) Bath surface; (16) Clean bath area; (17) Side extension.

Full Title Citation Front Review Classification Date Reference State Claims KMC Draw Desc

# ☐ 15. Document ID: FI 110302 B1, NO 9604895 A, SE 9704014 A, FI 9704230 A, DK 9701284 A, SE 517651 C2

L11: Entry 15 of 27

File: DWPI

Dec 31, 2002

DERWENT-ACC-NO: 1998-345907

DERWENT-WEEK: 200311

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TITLE: Shower unit with basin on floor surface - is with or without shower walls,

basin having bottom located relatively close to floor surface

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 1996NO-0004895 (November 18, 1996)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
FI 110302 B1	December 31, 2002		000	A47K003/02
NO 9604895 A	May 19, 1998		000	A47K003/22
SE 9704014 A	May 19, 1998		`001	A47K003/22
FI 9704230 A	May 19, 1998		000	A47K003/02
DK 9701284 A	May 19, 1998		000	E03C001/01
SE 517651 C2	July 2, 2002		000	A47K003/22

INT-CL (IPC):  $\underline{A47}$  K  $\underline{3/02}$ ;  $\underline{A47}$  K  $\underline{3/022}$ ;  $\underline{A47}$  K  $\underline{3/22}$ ;  $\underline{E03}$  C  $\underline{1/01}$ ;  $\underline{E03}$  C  $\underline{1/02}$ 

Full	Title Citation	Front Review	Classification D	ate Reference		Claims KWC	Draw, Desi
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	16. Docur	nent ID: SE 5	504534 <b>C</b> 2				
L11:	Entry 16 of	£ 27		File:	DWPI	Mar 3	, 1997

DERWENT-ACC-NO: 1997-243390

DERWENT-WEEK: 199722

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TITLE: Support basket maintaining filter hose tensioned in filter - involves hose open at one end and closed at other and, having at least two radially directed vanes extending in its longitudinal direction

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 1996SE-0001281 (April 3, 1996)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 SE 504534 C2
 March 3, 1997
 010
 B01D046/06

INT-CL (IPC): B01 D 46/06

ABSTRACTED-PUB-NO: SE 504534C

BASIC-ABSTRACT:

The radially directed vanes (13) has longitudinal edges (15) turned towards the hose

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.12&ref=11&dbname=PGPB,USPT,U... 10/27/04

interior (14) and components (16) for maintaining engagement with the hose interior. The engagement components are formed along the whole or parts of the vane longitudinal edges, and have the shape of projecting protuberances (17) engaging with the interior of the filter hose (5). The protuberances are sawtooth-like barbs (17), are equal in size or at least some of them extend further than the rest, inclined in the direction of the filter house open end (11). The vanes cross each other and are assembled or made in one piece with one another. They are essentially flat and relatively thin components of plastic or similar recyclable material. Through recesses (18) are provided in the vanes.

USE - To maintain a filter hose in a tensioned state in a filter.

ADVANTAGE - The support basket is very simple and cheap to make, is of one-time usage and can be simply recycled. (Reissue of the entry advised in week 9715 based on complete specification).

Full Title Citation Front Review Classificati	on Date Reference	Claims KWC Draw Desc
☐ 17. Document ID: SE 9403228	A, SE 506459 C2	Mar 27, 1996

DERWENT-ACC-NO: 1996-250343

DERWENT-WEEK: 199805

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TITLE: Abdominal muscle training machine - comprises seat part, back support part and foot support with main arm pivotable against effect of counter loading device

INVENTOR: ERIKSSON, B; ERIKSSON, C

PRIORITY-DATA: 1994SE-0003228 (September 26, 1994)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 SE 9403228 A
 March 27, 1996
 000
 A63B023/02

 SE 506459 C2
 December 15, 1997
 000
 A63B023/02

INT-CL (IPC): A63 B 23/02

ABSTRACTED-PUB-NO: SE 9403228A

BASIC-ABSTRACT:

The main arm of the abdominal muscle training machine is connected to a cross arm (16) which is activated by a training person bending the trunk forwards and locating his or her chest against it. The back support part (3) is longer than the seat part (2) and has a convexly bowed locating surface (10) for the back of the training person.

The plane of the two parts extend at an obtuse angle towards each other. In the area of the foot support (4) is arranged a foot-operated regulator (24) which via a transmission (28) is connected with the main arm, making possible the removal of the cross arm from the back support part without manual activation of the cross arm itself.

Full Title Citation From	et Pavison Classification	Date Reference	Claims KVMC Draw Desi
Full Title Citation Flor	Life Dealers   Sieppingerian		······································

☐ 18. Document ID: SE 9300712 A, SE 509482 C2

L11: Entry 18 of 27

File: DWPI

Sep 5, 1994

DERWENT-ACC-NO: 1994-355767

DERWENT-WEEK: 199911

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TITLE: Arrangement with hose filter - filters air contaminated with particles, and involves housing with lower inlet chamber for dirty air and upper outlet chamber for discharge of filtered air

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 1993SE-0000712 (March 4, 1993)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 SE 9300712 A
 September 5, 1994
 010
 B01D029/17

 SE 509482 C2
 February 1, 1999
 000
 B01D029/17

INT-CL (IPC): B01D 29/17; B01D 46/06

ABSTRACTED-PUB-NO: SE 9300712A

BASIC-ABSTRACT:

The inlet and outlet chambers (8, 9) are sepd. from one another by means of a sepg. wall (6). One or more filter hoses (5) are suspended in the sepg. wall (6) centrally to their recesses (7) and which each at its lower end (10) is closed by a crossways closure component (11). At their upper end (12) they are open for connection to the outlet chamber (9) via the corresp. recess (7) in the sepg. wall (6). Each filter hose (6) on its length is closed by means of a longitudinal closure component (13) and accommodates a support component (14) to hold the filter hose (5) tensioned. The support component comprises a sprung construction locating against a filter hose (15), which extends between the hose lower and upper ends (10, 12). Each filter hose at its lower end has at least two parallel spaced apart, crossways closure components (11), which between them limit a crossways channel (20) through which is passed a fixation component (12) for fixing filter hoses in a row in line with each other.

USE - As a hose filter.

ADVANTAGE - The arrangement permits an increased movement of the filter hoses during clean blowing, etc., and thereby an improved cleaning.

Full Ti	itle Citation Front Review Clas	sification Date Reference	Claims KMC Draw Desc
	9. Document ID: SE 9103	502 A	anamananan makaman mak
	ntry 19 of 27	File: DWPI	Jun 4, 1993

DERWENT-ACC-NO: 1993-293367

DERWENT-WEEK: 199337

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TITLE: Movement value recorder for muscle training appts. with elements movable to=and=fro against gravity - has load monitor supplying signals to computer for processing and/or storing internally or on separate data carrier

INVENTOR: ERIKSSON, B; ERIKSSON, C

PRIORITY-DATA: 1991SE-0003593 (December 3, 1991)

PATENT-FAMILY:

PUB-NO PUB-DATE LANGUAGE PAGES MAIN-IPC

SE 9103593 A June 4, 1993 015 A63B024/00

INT-CL (IPC): A63B 24/00

ABSTRACTED-PUB-NO: SE 9103593A

BASIC-ABSTRACT:

The load monitor comprises a wt. monitor fitted on a pick-up element to register the position of a lock unit for retaining a selectable number of weights on the pick-up element. The wt. monitor is in the form of a long element on which a series of indication elements is arranged. Every other element comprises a LED which emits a light beam in at least two opposite directions. The remaining elements comprise two pair-mounted phototransistors. The position of the lock unit is monitored by its breaking the light beam within an interval between a LED and an adjacent phototransistor.

USE - Recording movements, such as stroke length, angle deflection, load or similar.

Full	Title	Citation Front	Review	Classification	Date	Reference		Claims	KMC	Draw, Desc
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	20.	Document I	D: SE 9	102959 A						
1.11:	Entry	, 20 of 27				File:	DWPI	Apr	12,	1993

DERWENT-ACC-NO: 1993-203687

DERWENT-WEEK: 199325

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TITLE: Driving mat for tee on golf course - can also be used on indoor and outdoor driving ranges and consists of long tight brush bunches of two degrees of hardness

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 1991SE-0002959 (October 11, 1991)

PATENT-FAMILY:

 PUB-NO
 PUB-DATE
 LANGUAGE
 PAGES
 MAIN-IPC

 SE 9102959 A
 April 12, 1993
 000
 A63B069/36

INT-CL (IPC): A63B 69/36

ABSTRACTED-PUB-NO: SE 9102959A

BASIC-ABSTRACT:

The driving mat for a golf course or driving range is based on long tightly located brush bunches mounted on plates and having two degrees of hardness. They are in turn mounted on slide rails. It incorporates a peg arrangement which reduces the risk of accidents on the practice field and muscle damage which can occur during training.

USE/ADVANTAGE - A driving mat for the tee on a golf course green and which can also be used on a driving range in or out of doors.

## ☐ 21. Document ID: SE 9102315 A, SE 503403 C2

L11: Entry 21 of 27

Feb 9, 1993

DERWENT-ACC-NO: 1993-107521

DERWENT-WEEK: 199629

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TITLE: Muscle training machine - comprises frame in which is mounted counter load

device with the movable set of weights connected to draw line

INVENTOR: ERIKSSON, B; ERIKSSON, C

PRIORITY-DATA: 1991SE-0002315 (August 8, 1991)

PATENT-FAMILY:

PUB-DATE LANGUAGE PAGES MAIN-IPC PUB-NO 000 A63B021/06 February 9, 1993 SE 9102315 A 000 A63B021/06 SE 503403 C2 June 10, 1996

INT-CL (IPC): A63B 21/06

ABSTRACTED-PUB-NO: SE 9102315A

BASIC-ABSTRACT:

The draw line (3) has a free grippable end (14) and is arranged to run around a number of break wheels of which a first (17) is fitted on a holder (18) adjustable movable and lockable in different height positions in relation to the frame. In this way, the line free end can be drawn outwards at different levels in relation to the frame.

Apart from the first holder connected wheel, the machine has two separate second and third such wheels (19,20) from which the line runs in a loop laid around a fourth break component (21). One of the break wheels guides the line in a part running to a fifth break component (22) where it evolves into an end part (3') firmly connected to the holder (18).

USE/ADVANTAGE - For the specific training of muscles in the human body.

Full Title	Citation Front	Review	Classification	Date	Reference		Claims	KOME	Draw, Desc
	·								
□ 22.	Document II	): SE 9	102314 A,	SE 46	69587 B				
L11: Entry	22 of 27				File:	DWPI	Fe	b 9,	1993

DERWENT-ACC-NO: 1993-107520

DERWENT-WEEK: 199313

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TITLE: Muscle training machine - comprises counter loading device mounted in frame

with at least one set of weights connected to line

INVENTOR: ERIKSSON, B; ERIKSSON, C

PRIORITY-DATA: 1991SE-0002314 (August 8, 1991)

PATENT-FAMILY:

LANGUAGE PAGES MAIN-IPC PUB-DATE PUB-NO A63B021/00 000 SE 9102314 A February 9, 1993 A63B021/00 000 SE 469587 B August 2, 1993

INT-CL (IPC): A63B 21/00

ABSTRACTED-PUB-NO: SE 9102314A

BASIC-ABSTRACT:

The line (3) or similar is withdrawable from a specific point (10) at a distance from which is located a column (17) with which is connected a rotatable support unit (18) against which a training person can apply the desired part of their body, e.g. an arm, so that by pulling on the line an exactly repeatable and isolated training of just one specific muscle or muscle group is achieved.

USE/ADVANTAGE - For training of specific body muscles.

Full Tit	e Citation From	nt Review Class	ification Date	Reference			Claims	Koole	Drawi Desi
	<b></b>		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		······································				······
23	B. Document	ID: SE 46773	89 B, RU 20	)94999 <b>C</b> 1	, WO 9217	7503 A1, SI	E 92006	649 <b>A</b> ,	AU
921422	1 A, FI 93043	42 A, NO 9303	3507 A, EP	578661 A	.1, JP 0650	5982 W, U	S 54118	387 A,	EP
578661	B1, DE 69213	3724 E, ES 209	94904 T3						

L11: Entry 23 of 27

File: DWPI

Sep 7, 1992

DERWENT-ACC-NO: 1992-321544

DERWENT-WEEK: 199826

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TITLE: Prodn. and use of collagen - in which animal intestines with base material are mixed with ice water at pH 5.5, heated and hydrolysed at pH 10.5 using proteolytic enzyme

INVENTOR: SJOELANDER, E; ERIKSSON, C

PRIORITY-DATA: 1991SE-0000999 (April 5, 1991)

### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
SE 467739 B	September 7, 1992		010	C07K003/28
RU 2094999 C1	November 10, 1997		004	A22C013/00
WO 9217503 A1	October 15, 1992	E .	014	C07K015/20
SE 9200649 A	October 6, 1992		000	с09H009/00
AU 9214221 A	November 2, 1992		000	C07K015/20
FI 9304342 A	October 4, 1993		000	C07K000/00
NO 9303507 A	September 30, 1993		000	С07К003/28
EP 578661 A1	January 19, 1994	E	000	C07K015/20
JP 06505982 W	July 7, 1994		006	C07K015/20
US 5411887 A	May 2, 1995		004	C07K001/14
EP 578661 B1	September 11, 1996	E	005	C07K014/78
DE 69213724 E	October 17, 1996		000 .	C07K014/78

INT-CL (IPC):  $\underline{A22}$   $\underline{C}$   $\underline{13/00}$ ;  $\underline{A23}$   $\underline{L}$   $\underline{1/317}$ ;  $\underline{A61}$   $\underline{K}$   $\underline{38/39}$ ;  $\underline{A61}$   $\underline{L}$   $\underline{15/32}$ ;  $\underline{B65}$   $\underline{B}$   $\underline{25/06}$ ;  $\underline{C07}$   $\underline{K}$ 0/00; C07 K 1/14; C07 K 1/36; C07 K 3/02; C07 K 3/10; C07 K 3/28; C07 K 14/435; C07 K 14/78; co7 K 15/20; co9 D 7/12; co9 H 9/00; D06 N 3/00; H01 L 23/29

ABSTRACTED-PUB-NO: EP 578661B BASIC-ABSTRACT:

Native collagen is produced from animal intestines, stomach, rumen, lungs and udders, and the base material is cleaned and immersed inice water, with the pH regulated to approximately 5.5. The mixt. of base material and ice water is ground, and then fuether water is added so that the ground mixt. contains approximately equal wt. parts of base material and water.

The mixt. is then heated to 40-42 deg.C and the pH is regulated to pref. 10.5, after which a proteolytic enzyme is added in an amt. corresp. to 50 Anson units per kg so that hydrolysis of proteins other than collagen takes place, maintaining the pH value by addition of alkali until the hydrolysis is ready and the alkali is no longer consumed.

The pH is then regulated to 5.5. by the addn. of acid, and then the sepd. collagen is removed and used. The pH is regulated at al stages with the aid or hydrochloric acid, citric acid or lactic acid.

ADVANTAGE - The prodn. of collagen from animal internal organs ABSTRACTED-PUB-NO:

### SE 467739B EQUIVALENT-ABSTRACTS:

Process for the production of native collagen from intestines, stomach, skin hides, characterised by the following process steps: (a) the starting materials are cleaned and immersed in ice-water, the pH is regulated to about 5.5, (b) the mixture of starting materials and ice-water is ground whereupon further water is added so that the ground mixture contains about equal weight parts of starting materials and water, (c) the mixture is heated to 40-42 degrees C and pH is regulated to at most 11, preferably 10.5 whereupon a proteolytic enzyme, in an amount corresponding to 60 Anson units per kilogram solids is added so that hydrolyses of other proteins than collagen occurs when maintaining the pH-value by adding alkali until the hydrolyses is completed and the alkali is no longer consumed, whereupon (d) pH is regulated to 5.5 by the addition of an acid, whereupon (e) collagen is separated and collected.

### US 5411887A

L11: Entry 24 of 27

Collagen is sepg from animal tissue by immersing the tissue in a mixt of frozen and lig water whose pH is about 5.5 and heating it to no higher than 42 deg C while regulating the pH to keep it below 11. At least one proteolytic enzyme is then added to hydrolyse protein, other than collagen. The pH is adjusted back to 5.5 before sepg the collagen.

Pref additional water is added to the water collagen mixt to make it 50 wt% water and 50 wt% collagen. Pref hydrochloric, citric or lactic acid is used to keep the pH down to 5.5 and NaOH to keep pH up to 11. The hydrolysing takes 1.75-3.5 hours.

USE - Sepg collagen form slaughtered animal tissue, eg intestines and stomach.

Full	Title	Citation	Front	Review	Classification	Date	Reference		Clair	ns KWC	D raw.	Desc
								,				
									 		***************************************	
	24.	Docume	ent ID	: WO	9100918 A							

File: DWPI

Jan 24, 1991

DERWENT-ACC-NO: 1991-051342

DERWENT-WEEK: 199107

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TITLE: Phospho:lipid with 2-carboxylic acid substituent prepn. - by esterifying lysophospholipid with relevant carboxylic acid in presence of phospholipase A2 catalyst

in micro:emulsion

INVENTOR: EKSTRAND, B; ERIKSSON, C; HOLMBERG, K; OSTERBERG, E

PRIORITY-DATA: 1989WO-SE00409 (July 12, 1989), 1990WO-SE00481 (July 4, 1990)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

**PAGES** 

MAIN-IPC

WO 9100918 A

January 24, 1991

000

INT-CL (IPC): C11C 3/08; C12P 7/64

ABSTRACTED-PUB-NO: WO 9100918A

BASIC-ABSTRACT:

A method for the prepn of a phospholipid with a carboxylic acid residue in the alphaposition comprises esterifying a lysophospholipid with a corresponding carboxylic acid in the presence of phospholipase A2 catalyst. The esterification takes place in a microemulsion with a water content of 0.1-2 wt%. also claimed is a phospholipid characterised by a W-3-fatty acid residue in the 2-position.

 ${\tt USE/ADVANTAGE\ -\ The\ phospholipid\ comprising\ W-3-fatty\ acid\ residue\ in\ the\ 2-position}$ are useful for treating people having increased risk of thrombosis and infarct of the heart. The prod is taken up more efficiently by the body since np metabolism of the phospholipid takes place. The inventure method affords the W-3-fatty acid subst phospholipid.

Full   Title   Citation   Front   Review   Classification   Date   Reference	aims KMC Draw. Des

25. Document ID: SE 459156 B 

L11: Entry 25 of 27

File: DWPI

Jun 12, 1989

DERWENT-ACC-NO: 1989-307222

DERWENT-WEEK: 198942

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TITLE: Stop unit for wt. training appts. - inserts between two weights and locks on bar carrying stacked weights, and has two arms pivotable around common joint

INVENTOR: ERIKSSON, B; ERIKSSON, C

PRIORITY-DATA: 1988SE-0002477 (July 1, 1988)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

SE 459156 B

June 12, 1989

008

INT-CL (IPC): A63B 21/06

ABSTRACTED-PUB-NO: SE 459156B

### BASIC-ABSTRACT:

The training appts. comprises several weights arranged one on top of the other, with a variable number of them lockable by the stop unit (1) on at least one bar inserted through holes in the weights. The bar has a number of separate tracks or recesses. When the stop unit is inserted between two adjacent weights, it engages in one of the tracks so that all weights located above it follow the bar when it is lifeted by the efforts of a person training.

The stop unit comprises two arms (2'2") pivotable around a common joint (3), and activated by at least one spring unit (4) so that the stop unit is maintained in engagement with the track. The spring unit comprises a screw draw spring with a dual function, holding the stop unit together by maintaining the arms pressed into the track, and also allowing them to pivot outwards against the effect of spring force to return to the closed position.

USE/ADVANTAGE - For wt. training activities, to obviate problems and delays inherent in the changing wt. loadings for different persons training.

Full Title C	itation Front	Review	Classification	Date	Reference		Claims	KMAC	Draw Desi
***************************************							 		
	) ID	. CEO	101020 A						
□ 26. I	Document ID	7. SE 8	101838 A						
L11: Entry	26 of 27		٠.		File:	DWPI	Oct	25,	1982

DERWENT-ACC-NO: 1982-P7584E

DERWENT-WEEK: 198245

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TITLE: Roof installation method - involves using two different module blocks, one

overlapping other at roof ridge

INVENTOR: ERIKSSON, C; PAULSSON, A; SAMUELSSON, S

PRIORITY-DATA: 1981SE-0001838 (March 23, 1981)

PATENT-FAMILY:

PUB-NO PUB-DATE LANGUAGE PAGES MAIN-IPC

SE 8101838 A October 25, 1982 000

INT-CL (IPC): E04D 11/00

ABSTRACTED-PUB-NO: SE 8101838A

BASIC-ABSTRACT:

The method is for installation of a roof using two different types of prefabricated module blocks (la,lb). The first module, at the roof ridge, rests on the top edge of the other. The two types of module blocks are arranged alternatively.

To fix the blocks at the roof foot, anchoring fitments are used which have projecting tongues of bendable material, such as relatively soft steel. These tongues are inserted under the contact parts on the roof foot fitments, so that they are bent when the module blocks ae raised.

Fuil Title	Citation	Front	Review	Classification	Date Referenc	e	Claims	KWMC	Draw, Desi

L11: Entry 27 of 27 File: DWPI Aug 7, 1980

DERWENT-ACC-NO: 1980-H3973C

DERWENT-WEEK: 198034

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TITLE: Guide for relatively movable machine components - has sliding surfaces

separated by flat and spherically curved surfaces to prevent jamming

INVENTOR: ERIKSSON, C

PRIORITY-DATA: 1979SE-0000910 (February 2, 1979)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

WO 8001547 A

August 7, 1980

Е

000

SE 7900910 A

September 1, 1980

000

INT-CL (IPC): B23B 49/00; B23Q 15/20; B25J 17/00; B25J 19/00; F16C 23/00; F16C 31/00

ABSTRACTED-PUB-NO: WO 8001547A

BASIC-ABSTRACT:

The two outer parts are relatively movable, an intermediate part keeping an imaginary reference line of the outer parts parallel. Between one of the outer parts and the adjoining intermediary surface is provided a flat boundary surface. Between the other outer part and the intermediate part, a spherical boundary surface is provided.

The centre of curvature of the boundary surface coincides with point located a distance from the assembly to which the reference lines constantly point. Relative movement between the parts lying adjacent to each other is effected by sliding between the surfaces.

Full Title Citation Front Review	v   Classification   Date   Referen	ce Signature	Claims KMC Draw. De
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Terms		Documents	
Eriksson-C.IN.			27

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**Generate OACS Generate Collection** Print Fwd Refs **Bkwd Refs** Clear Search Results - Record(s) 1 through 1 of 1 returned. 1. Document ID: EP 1228195 A1, WO 200130981 A1, AU 200111692 A Using default format because multiple data bases are involved. Aug 7, 2002 File: DWPI L14: Entry 1 of 1 DERWENT-ACC-NO: 2001-335700 DERWENT-WEEK: 200259 COPYRIGHT 2004 DERWENT INFORMATION LTD TITLE: New in vitro adhesion culture of glial fibrillary acidic protein immunoreactive (GFAP positive) cells useful for proliferating and differentiating GFAP positive nestin positive cells for transplantation to patients with Parkinson's disease INVENTOR: CAMPBELL, K; ERIKSSON, C; FAGERSTROM, C; WAHLBERG, L; WICTORIN, K PRIORITY-DATA: 2000US-0161316 (October 24, 2000), 1999US-161316P (October 25, 1999) PATENT-FAMILY: PUB-DATE LANGUAGE PAGES MAIN-IPC PUB-NO 000 C12N005/06 August 7, 2002 EP 1228195 A1 May 3, 2001 064 C12N005/06 WO 200130981 A1 C12N005/06 000 May 8, 2001 AU 200111692 A INT-CL (IPC): A61 K 35/30; A61 K 48/00; C12 N 5/06; C12 N 5/08; C12 N 5/10; C12 N 5/16; G01 N 33/48 Citation Front Review Classification Date Reference Generate OACS Print **Fwd Refs Bkwd Refs** Clear Generate Collection Documents Terms Wictorin-K.IN. Change Format Display Format:

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## Search Results - Record(s) 1 through 6 of 6 returned.

## ☐ 1. Document ID: US 4575608 A

# Using default format because multiple data bases are involved.

L15: Entry 1 of 6

File: USPT

Mar 11, 1986

US-PAT-NO: 4575608

DOCUMENT-IDENTIFIER: US 4575608 A

TITLE: Method and apparatus for spot heating a body, particularly for brazing hard

solder gold alloys

DATE-ISSUED: March 11, 1986

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Wictorin; Lennart S-131 50 Saltsjo-Duvnas SE Carlberg; Torbjorn S-191 76 Sollentuna SE

Liljendahl; Mikael S-161 54 Bromma SE

US-CL-CURRENT: 219/85.13; 219/85.12, 219/85.17, 392/421

Full Title Citation Front Review Classification Date Reference Claims KMC Draw Des

## ☐ 2. Document ID: WO 9530402 A1

L15: Entry 2 of 6

File: EPAB

Nov 16, 1995

PUB-NO: WO009530402A1

DOCUMENT-IDENTIFIER: WO 9530402 A1 TITLE: PHOTOPOLYMERIZABLE COMPOSITION

PUBN-DATE: November 16, 1995

INVENTOR-INFORMATION:

NAME COUNTRY

WICTORIN, LENNART SE
LARSSON, ANDERS SE

INT-CL (IPC): A61 K 6/087

EUR-CL (EPC): A61K006/087; C08G059/24, C08G059/68 , C08G059/68 , C08L063/00

### ABSTRACT:

CHG DATE=19990617 STATUS=0>A photopolymerizable epoxy-monomer, preferably 3,4-epoxycyclohexyl-methyl-3,4-epoxy-cyclohexane-carboxylate or bis-(3,4-epoxycyclohexyl-adipate) is included in photo-hardening compositions, preferably for dental use. The

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.16&ref=15&dbname=PGPB,USPT,U... 10/27/04

compositions exhibit no hardening shrinkage, or very little hardening shrinkage, and high mechanical strength.

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Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	KOMU	Draw, Desc
5.618	1111	- Ottomoni	1 10/11		0.000				 		<u> </u>

# ☐ 3. Document ID: EP 1228195 A1, WO 200130981 A1, AU 200111692 A

L15: Entry 3 of 6

File: DWPI

Aug 7, 2002

DERWENT-ACC-NO: 2001-335700

DERWENT-WEEK: 200259

COPYRIGHT 2004 DERWENT INFORMATION LTD

TITLE: New in vitro adhesion culture of glial fibrillary acidic protein immunoreactive (GFAP positive) cells useful for proliferating and differentiating GFAP positive nestin positive cells for transplantation to patients with Parkinson's disease

INVENTOR: CAMPBELL, K; ERIKSSON, C; FAGERSTROM, C; WAHLBERG, L; WICTORIN, K

PRIORITY-DATA: 2000US-0161316 (October 24, 2000), 1999US-161316P (October 25, 1999)

### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1228195 A1	August 7, 2002	E	000	C12N005/06
WO 200130981 A1	May 3, 2001	E	064	C12N005/06
AU 200111692 A	May 8, 2001		000	C12N005/06

INT-CL (IPC):  $\underline{A61}$   $\underline{K}$   $\underline{35/30}$ ;  $\underline{A61}$   $\underline{K}$   $\underline{48/00}$ ;  $\underline{C12}$   $\underline{N}$   $\underline{5/06}$ ;  $\underline{C12}$   $\underline{N}$   $\underline{5/08}$ ;  $\underline{C12}$   $\underline{N}$   $\underline{5/10}$ ;  $\underline{C12}$   $\underline{N}$   $\underline{5/10}$ ;  $\underline{C12}$   $\underline{N}$ 

ABSTRACTED-PUB-NO: WO 200130981A

BASIC-ABSTRACT:

NOVELTY - An in vitro adhesion cell culture of glial fibrillary acidic protein immunoreactive (GFAP+) cells, is new.

DETAILED DESCRIPTION - An in vitro adhesion cell culture GFAP+ cells, where:

- (a) one or more cells in the culture have the capacity to differentiate into neurones;
- (b) the cell culture divides in a culture medium containing serum (S) and at least one proliferation-inducing growth factor (PGF), and
- (c) one or more cells (I) in the culture have the capacity to differentiate into neurons, upon withdrawal of both (S) and PGF.

INDEPENDENT CLAIMS are also included for the following:

- (1) an in vitro cell culture (I) consisting essentially of a culture medium containing (S) and PGF, and cells derived from the central nervous system of a mammal, where the cells in the culture are GFAP+, capable of proliferating in a culture medium containing (S) and PGF, and capable of differentiating into neurons in the absence of both the (S) and PGF from the culture medium;
- (2) producing (P1) a neuronal cell in vitro, by obtaining neural tissue from a http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.16&ref=15&dbname=PGPB,USPT,U... 10/27/04

mammal, the neural tissue containing at least one GFAP+ cell capable of producing progeny that is a GFAP+ cell, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate GFAP+ cell and produce a GFAP+ cell progeny, and differentiating the cell progeny in a second culture medium that is substantially free of both the (S) and PGF;

- (3) producing (P2) a non-neuronal cell in vitro, by P1, and differentiating the cell progeny in a second culture medium that is substantially free of (S);
- (4) producing (P3) a genetically modified GFAP+ cell, by P1, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (5) producing (P4) a genetically modified differentiated neural cell culture, by P1, and differentiating the cell progeny to contain at least 10% neurons in a second culture medium that is substantially free of both the (S) and PGF, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (6) producing (P5) a genetically modified non-neuronal cell culture, by P1, and differentiating the cell progeny to contain at least 10% glia in a second culture medium that is substantially free of (S), where the glia are GFAP+ and vimentin positive, and genetically modifying the non-neuronal cell;
- (7) transplanting GFAP+ nestin+ cell progeny to a host, by obtaining neural tissue from a mammal, the neural tissue containing at least one GFAP+ nestin+ cell capable of producing progeny that are capable of differentiating into neurons and glia, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ nestin+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate the GFAP+ nestin+ cell and produce GFAP+ nestin+ cell progeny, and transplanting the GFAP+ nestin+ cell progeny to the host;
- (8) determining the effect of at least one biological agent on a GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell progeny by the above said method, contacting the proliferated GFAP+ nestin+ cell with the biological agent, and determining the effect of biological agent on GFAP+ nestin+ cells;
- (9) determining the effect of at least one biological agent on the differentiation of GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said method, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate in a second culture medium in the presence of biological agent, and determining the effects of the biological agent on the differentiation of the GFAP+ nestin+ cells;
- (10) determining the effect of at least one biological agent on the differentiated GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said process, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate into neurons or glia, contacting the differentiated neural cells with the biological agent, and determining the effects of the biological agent on the differentiated neural cells;
- (11) a cDNA library prepared from (I); and
- (12) a cell population consisting essentially of isolated GFAP+ nestin+ cells.

ACTIVITY - Immunosuppressive; antiparkinsonian.

No supporting biological data given.

MECHANISM OF ACTION - None given.

USE - The culture method is useful for proliferating and differentiating GFAP+ nestin+ cells (claimed). The cultured cells are useful for transplantation procedures, particularly to patients suffering from Parkinsonian's disease.

4. Document ID: WO 9530402 A1, DE 69519038 E, SE 9401558 A, AU 9524591 A, SE 502812 C2, EP 788344 A1, EP 788344 B1

L15: Entry 4 of 6

File: DWPI

Nov 16, 1995

DERWENT-ACC-NO: 1995-403920

DERWENT-WEEK: 200064

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TITLE: Low shrinkage photopolymerisable dental filler - based on ring-contg. di:epoxide(s), esp. 3,4-epoxy:cyclo:hexyl-methyl-3,4-epoxy-cyclohexane, carboxylate or bis (3,4-epoxy:cyclo:hexyl) adipate

INVENTOR: LARSSON, A; WICTORIN, L ; JOENSSON, S E

PRIORITY-DATA: 1994SE-0001558 (May 5, 1994)

### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9530402 A1	November 16, 1995	E	019	A61K006/087
DE 69519038 E	November 9, 2000		000	A61K006/087
SE 9401558 A	November 6, 1995		000	A61K006/087
AU 9524591 A	November 29, 1995		000	A61K006/087
SE 502812 C2	January 22, 1996		000	A61K006/087
EP 788344 A1	August 13, 1997	E	000	A61K006/087
EP 788344 B1	October 4, 2000	Е	000	A61K006/087

INT-CL (IPC): A61 K 6/087

ABSTRACTED-PUB-NO: EP 788344B

BASIC-ABSTRACT:

A photopolymerisable dental filling compsn. is based on monomers of formula (I), esp. 3,4-epoxycyclohexyl-methyl-3,4-epoxy-cyclohexane-carbox- ylate (IA) or bis-(3,4epoxycyclohexyl)-adipate (IB) A,B and C = 0-10 (pref. 0-2) atom chain; X = -0-, -NH.CO-, -NH-, -CO- or a chemical band; and Y1 and Y2 = opt. substd. carboxylic, heterocyclic, aliphatic or aromatic ring of 5, 6 or 7 ring atoms.

ADVANTAGE - The compsns. show low shrinkage (eg. 0.08-0.17 linear %) on curing with UV or visible light, white (I) show low index values in skin irritation tests (eg. 0.5 in a 0-8 index scale). ABSTRACTED-PUB-NO:

### WO 9530402A EQUIVALENT-ABSTRACTS:

A photopolymerisable dental filling compsn. is based on monomers of formula (I), esp. 3,4-epoxycyclohexyl-methyl-3,4-epoxy-cyclohexane-carbox- ylate (IA) or bis-(3,4epoxycyclohexyl)-adipate (IB) A,B and C = 0-10 (pref. 0-2) atom chain; X = -0-, -NH.CO-, -NH-, -CO- or a chemical band; and Y1 and Y2 = opt. substd. carboxylic, heterocyclic, aliphatic or aromatic ring of 5, 6 or 7 ring atoms.

ADVANTAGE - The compsns. show low shrinkage (eg. 0.08-0.17 linear %) on curing with UV or visible light, white (I) show low index values in skin irritation tests (eg. 0.5 in a 0-8 index scale).

## ☐ 5. Document ID: SE 8002785 A

L15: Entry 5 of 6

File: DWPI

Nov 16, 1981

DERWENT-ACC-NO: 1982-11178E

DERWENT-WEEK: 198206

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TITLE: Gold alloy for use in dental technology - contains cobalt and opt. chromium

and molybdenum

INVENTOR: FREDRIKSSO, H; WICTORIN, L

PRIORITY-DATA: 1980SE-0002785 (April 14, 1980)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

SE 8002785 A

November 16, 1981

003

INT-CL (IPC): C22C 5/02

ABSTRACTED-PUB-NO: SE 8002785A

BASIC-ABSTRACT:

Dental alloy comprises 90 wt.% gold and 10 wt.% cobalt. The alloy can be heat treated to various hardness es. to approx. 200 Hv, and the presence of only two elements prevents inhomogeneous structure and corrosion.

A second dental alloy comprises 75-80 wt.% gold 0-10wt.% Cobalt, 0-10% chromium, and/or 0-5 wt.% Molybdenum and 0-5 wt.% Palladium, to which a porcelain layer can be fired. The alloy heat treatment comprises a soln. stage at 850-930 deg.C followed by hardening at 100-400 deg.C and rapid cooling. (Provisional Basic previously advised in Week D49).

Full Title Citation Front Review Clas	sification Date Reference	Claims KMC Draw Desc
☐ 6. Document ID: US 375265	54 A	
L15: Entry 6 of 6	File: USOC	Aug 14, 1973

US-PAT-NO: 3752654

DOCUMENT-IDENTIFIER: US 3752654 A

TITLE: ABSORPTION UNIT FOR THE ABSORPTION OF CARBON DIOXIDE

DATE-ISSUED: August 14, 1973

US-CL-CURRENT: 422/120; 128/205.28, 96/118

DOCUMENT TEXT:

Aug. 14, 1973 31752,654@ D. O. A. JOHANNISSON ET AL ABSORPTIO"Q UNIT FOR THE ABSORPTION OF CARBON I) IOXIDE Filed Feb. 10; 1972 4- FIG.1 4 FIG. A? FIG.,5 10 "'I 4" 15 15

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.16&ref=15&dbname=PGPB,USPT,U... 10/27/04

3 1 7 5 2 @ 6 5 4 Utilted States Patent Office' Patented Aug. 14, 1973 3,752,654 ABSORPIION UNIT FOR THE ABSORPTION OF CARBON DIOXIDE Dag 0. A. Johannisson and Ake G. R. Wictorin, Lidingo, Sweden, assignors to Aga Aktiebolag, Lidingo, Sweden 5 Filed Feb. 10, 1972, Ser. No. 225,035 Claims priority, application Sweden, Feb. 15, 1971, 1,859/71 Int. Cl. Bold 53104, B01i 1114, A62b 7110 U.S. Cl. 23-284 6 Claims 10 ABSTRACT OF THE DISCLOSURE In an absorption unit for the absorption of carbon dioxide, especially for a breathing apparatus having a sub- 15 stantiahy closed gas system the space inside the unit is divided in a plurality of chambers, each one of which is filled with a carbon dioxide absorbing substance and bounded by walls of a porous material permitting the gas to pass from an inlet of the unit, through the walls and 20 the substance to an outlet of the unit. FIELD, OF THE INVENTION The present invention refers to an absorption unit for 25 the absorption of carbon dioxide of the kind which pref- erably can be used in a breathing apparatus having a sub- stantially closed gas system. BACKGROUND OF THE INVENTION 30 In a breathing apparatus having a substantially closed gas system breathing gas is caused to circulate while car- bon dioxide is absorbed and oxygen added so that the oxygen which is supplied to a patient is compensated for. An absorption unit for that purpose comprises a cor, tainer 35 with an inlet and an outlet and holding a substance adapted for absorbing carbon dioxide. PRIOR ART 40 -In prior absorption units which have comprised a con- tainer, the entire interior of which has been filled with the carbon dioxide absorbing substance it has been pos- sible to obtain a tilne of use in the order of 2 hours, which means that after this time the carbon dioxide has been 45 able to pass through the absorption unit without being absorbed. Then the total amoiint of the carbon dioxide absorbing substance has not been consumed but the passage of carbon dioxide through the absorption unit has been enabled since the carbon dioxide absorbing properties 50 of this substance has been used up within certain chan- nels or passages inside the substance. SUMMA.RY OF THE INVENTION According to the present invention a much better exploi- 55 tation of the carbon dioxide absorbing substance can be achieved in the same time as only a smaller amount of this substance is needed. This result has been achieved in that the space inside the container is divided into a plurality of chambers, each one of which is filled with the carbon di-60 oxide absorbing substance and in all directions bounded by partitions made of a porous material, such as poly- ether foamed plastic. BRIEF DESCRIPTION OF, TH-E DRAWING 65 'fhe invention is described below with reference to the annexed drawing, in which FIG. I schematically shows a breathing apparatus with an absorption unit according to the invention, FIG. 2 shows a section of the abs6rption 70 2 unit and FIG. 3 shows a section perpendicular to the sec- tion of FIG. 2. DESCRIPTION OF THE PREFERRED EMBODIMENT The absorption unit is made of @a container I which is connected with a tube 4 leading to a patient over a breathmg in tube 2 and a breathing out tube 3. In the closed gas system which is formed by the container I and the tubes 2 and 3 chec@k valves 5 and 6 are inserte(I for controlling the direction of the gasffow inside the gas system. A conduit 7 for supplying fresh breathing gas intended for compensating for oxygen which has been used up by the patient is connected with the breathing in tube 2 and this conduit 7 is provided with a chec@k valve 8. Finally the gas system comprises a breathing bag 9 having variable volume, for instance a rubber bag which is connected with the inlet of the absorption unit 1. From FIGS. 2 and 3 it is seen that the absorption unit 1 within a cylin&ical outer wall 10 which is connected with a bottom 1,1 and closed by a lid 12 comprises a plurality of sector formed chambers 13, in this case twelve ambers, which surround a central, cylindricary formed amber 14. These chambers are bounded in all directions by partitions 15 of a porous material which preferably consists of polyether foamed plastic. Thus, the partitions form an outer annular part, an inner annular part and between these a plurality of radially directed partitions, in this case twelve partitions. FIG. 3 indicates that the porous material 15 also can form the bottom and the lid of the chambers 13 and 14, but it is also possible that the bottom 11 and the lid 12 of the container I may lie directly and sealingly against the outer annular part, the inner annular part and the radially directed partitions of the porous material. By this configuration of the absorption unit the result is obtained that it comprises a much smaller amount of the carbon dioxide absorbing substance compared with the prior absorption units. While the prior absorption units had to be filled with about 600 gr. of the carbon dioxide absorbing substance the unit according to the invention needs only about 450 gr. In spite of this the time of use has been

expanded from about 2 hours with the prior unit to about 31/2 hours with the unit according to the invention. Thus, a substantial improvement has been obtained in these two regards, and furthermore, the partitions of the porous material contributes to hold any dust emanating from the carbon dioxide absorbing substance. This substance may be of the type called "sodasorb" and consists of a granulate of sodiumhy&oxide-caustic potash. Preferably, the lid 12 is fastened to the cylindrical wall of the container so that a certain compression of the porous mate al in the partitions 15 is obtained, whereby a sufficient sealing is achieved between this porous material and the cylindrical wall and the plane bottom and lid of the container. Thereupon, the lid can be joined to the cylindrical wall by glueing since a used unit normally is disposed with and replaced by a fresh unit. It is claimed: 1. Absorption unit for the absorption of carbon dioxide, especially for a breathing apparatus having a substantially closed gas system, in which breathing gas is caused to circulate while carbon dioxide is absorbed and oxygen is added, comprising a container having an inlet and an outlet and holding a carbon dioxide absorbing substance, characterized in that the carbon dioxide absorbing substance is placed in a Plurality of chambers (13, 14) in the container (1, 10, 11, 12) which are separated from each other, whereas each chamber is bounded by partitions

3.752,654 (15) -of a -porous material which allows the gas to pass from the inlet, through the partitions and the- carbon dioxide absorbing substance to the outlet. 2. Absorption unit as claimed in claim I in which the partitions (15) are made of polyether foamed plastic. 1 3.: Absorption unit as claimed in claim 1, in which the container has a circular outer wall (10) and substantially plane bottom (11) and a plane lid (12). 4. Absorption unit as claimed in claims 2 and 3, in which the lid (12) is sealifigly fa8tened to the cylindrical outer wall (10) qnder compression of the porous material of the partitions (15). Absorptio . n unit@ as claimed in claim-3, in which the container is provided with a plurality of sector formed chambers (13) surrounding a central, cylindricaliy formed chamber (14). 6. Absorption unit as claimed in claim 3, in which the inlet and the outlet of the abgorption unit are arranged in the cylindrical outer wall of the container and diametrically with regard to each other.. 5 References Cited UNITED STATES PATENTS 3,464,186 9/1969 - Hankison et al - ----- 55-387 10 3,5166,867 3/1971 Dryden ----- 128-188 31615,233 10/1971 Dbening ----- -- 23-252 CHARLES N. HART, Primary Examiner U.S. Cl. X@R. 15 23-252; 55-387; 128-142.6

Full Title Citation Front Review	Classification	Date	Reference		Claims KOMC Draw	Des
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**Search Results -** Record(s) 1 through 6 of 6 returned.

☐ 1. Document ID: US 4575608 A

Using default format because multiple data bases are involved.

L15: Entry 1 of 6

File: USPT

Mar 11, 1986

SE

US-PAT-NO: 4575608

DOCUMENT-IDENTIFIER: US 4575608 A

TITLE: Method and apparatus for spot heating a body, particularly for brazing hard

solder gold alloys

DATE-ISSUED: March 11, 1986

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Wictorin: Lennart S-131 50 Saltsjo-Duvnas

S-191 76 Sollentuna . SE

Carlberg; Torbjorn S-191 76 Sollentuna

Liljendahl; Mikael S-161 54 Bromma SE

US-CL-CURRENT: 219/85.13; 219/85.12, 219/85.17, 392/421

Full Title Citation Front Review Classification Date Reference Classification Date Reference

☐ 2. Document ID: WO 9530402 A1

L15: Entry 2 of 6

File: EPAB

Nov 16, 1995

PUB-NO: WO009530402A1

DOCUMENT-IDENTIFIER: WO 9530402 A1 TITLE: PHOTOPOLYMERIZABLE COMPOSITION

PUBN-DATE: November 16, 1995

INVENTOR-INFORMATION:

NAME COUNTRY

WICTORIN, LENNART SE LARSSON, ANDERS SE

INT-CL (IPC): A61 K 6/087

EUR-CL (EPC): A61K006/087; C08G059/24, C08G059/68 , C08G059/68 , C08L063/00

ABSTRACT:

CHG DATE=19990617 STATUS=0>A photopolymerizable epoxy-monomer, preferably 3,4-epoxycyclohexyl-methyl-3,4-epoxy-cyclohexane-carboxylate or bis-(3,4-epoxycyclohexyl-adipate) is included in photo-hardening compositions, preferably for dental use. The

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.16&ref=15&dbname=PGPB,USPT,U... 10/27/04

compositions exhibit no hardening shrinkage, or very little hardening shrinkage, and high mechanical strength.

Full Title	Citation Fron	t Review	Classification	Date	Reference	Claims Koolo	Draw, Desc

# ☐ 3. Document ID: EP 1228195 A1, WO 200130981 A1, AU 200111692 A

L15: Entry 3 of 6

File: DWPI

Aug 7, 2002

DERWENT-ACC-NO: 2001-335700

DERWENT-WEEK: 200259

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TITLE: New in vitro adhesion culture of glial fibrillary acidic protein immunoreactive (GFAP positive) cells useful for proliferating and differentiating GFAP positive nestin positive cells for transplantation to patients with Parkinson's disease

INVENTOR: CAMPBELL, K; ERIKSSON, C; FAGERSTROM, C; WAHLBERG, L; WICTORIN, K

PRIORITY-DATA: 2000US-0161316 (October 24, 2000), 1999US-161316P (October 25, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1228195 A1	August 7, 2002	E	000	C12N005/06
WO 200130981 A1	May 3, 2001	E	064	C12N005/06
AU 200111692 A	May 8, 2001		000	C12N005/06

INT-CL (IPC): A61 K 35/30; A61 K 48/00; C12 N 5/06; C12 N 5/08; C12 N 5/10; C12 N 5/16; G01 N 33/48

ABSTRACTED-PUB-NO: WO 200130981A

BASIC-ABSTRACT:

NOVELTY - An in vitro adhesion cell culture of glial fibrillary acidic protein immunoreactive (GFAP+) cells, is new.

DETAILED DESCRIPTION - An in vitro adhesion cell culture GFAP+ cells, where:

- (a) one or more cells in the culture have the capacity to differentiate into neurones;
- (b) the cell culture divides in a culture medium containing serum (S) and at least one proliferation-inducing growth factor (PGF), and
- (c) one or more cells (I) in the culture have the capacity to differentiate into neurons, upon withdrawal of both (S) and PGF.

INDEPENDENT CLAIMS are also included for the following:

- (1) an in vitro cell culture (I) consisting essentially of a culture medium containing (S) and PGF, and cells derived from the central nervous system of a mammal, where the cells in the culture are GFAP+, capable of proliferating in a culture medium containing (S) and PGF, and capable of differentiating into neurons in the absence of both the (S) and PGF from the culture medium;
- (2) producing (P1) a neuronal cell in vitro, by obtaining neural tissue from a http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.16&ref=15&dbname=PGPB,USPT,U... 10/27/04

mammal, the neural tissue containing at least one GFAP+ cell capable of producing progeny that is a GFAP+ cell, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate GFAP+ cell and produce a GFAP+ cell progeny, and differentiating the cell progeny in a second culture medium that is substantially free of both the (S) and PGF;

- (3) producing (P2) a non-neuronal cell in vitro, by P1, and differentiating the cell progeny in a second culture medium that is substantially free of (S);
- (4) producing (P3) a genetically modified GFAP+ cell, by P1, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (5) producing (P4) a genetically modified differentiated neural cell culture, by P1, and differentiating the cell progeny to contain at least 10% neurons in a second culture medium that is substantially free of both the (S) and PGF, and genetically modifying the GFAP+ cell to express a biologically active agent;
- (6) producing (P5) a genetically modified non-neuronal cell culture, by P1, and differentiating the cell progeny to contain at least 10% glia in a second culture medium that is substantially free of (S), where the glia are GFAP+ and vimentin positive, and genetically modifying the non-neuronal cell;
- (7) transplanting GFAP+ nestin+ cell progeny to a host, by obtaining neural tissue from a mammal, the neural tissue containing at least one GFAP+ nestin+ cell capable of producing progeny that are capable of differentiating into neurons and glia, dissociating the neural tissue to obtain a cell suspension comprising the GFAP+ nestin+ cell, culturing the cell suspension in a first culture medium containing (S) and PGF to proliferate the GFAP+ nestin+ cell and produce GFAP+ nestin+ cell progeny, and transplanting the GFAP+ nestin+ cell progeny to the host;
- (8) determining the effect of at least one biological agent on a GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell progeny by the above said method, contacting the proliferated GFAP+ nestin+ cell with the biological agent, and determining the effect of biological agent on GFAP+ nestin+ cells;
- (9) determining the effect of at least one biological agent on the differentiation of GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said method, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate in a second culture medium in the presence of biological agent, and determining the effects of the biological agent on the differentiation of the GFAP+ nestin+ cells;
- (10) determining the effect of at least one biological agent on the differentiated GFAP+ nestin+ cell, by proliferating GFAP+ nestin+ cell by the above said process, and producing a GFAP+ nestin+ cell progeny, inducing the proliferated GFAP+ nestin+ cells to differentiate into neurons or glia, contacting the differentiated neural cells with the biological agent, and determining the effects of the biological agent on the differentiated neural cells;
- (11) a cDNA library prepared from (I); and
- (12) a cell population consisting essentially of isolated GFAP+ nestin+ cells.

ACTIVITY - Immunosuppressive; antiparkinsonian.

No supporting biological data given.

MECHANISM OF ACTION - None given.

USE - The culture method is useful for proliferating and differentiating GFAP+ nestin+ cells (claimed). The cultured cells are useful for transplantation procedures, particularly to patients suffering from Parkinsonian's disease.

# ☐ 4. Document ID: WO 9530402 A1, DE 69519038 E, SE 9401558 A, AU 9524591 A, SE 502812 C2, EP 788344 A1, EP 788344 B1

L15: Entry 4 of 6

File: DWPI

Nov 16, 1995

DERWENT-ACC-NO: 1995-403920

DERWENT-WEEK: 200064

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TITLE: Low shrinkage photopolymerisable dental filler - based on ring-contg. di:epoxide(s), esp. 3,4-epoxy:cyclo:hexyl-methyl-3,4-epoxy-cyclohexane, carboxylate or bis (3,4-epoxy:cyclo:hexyl) adipate

INVENTOR: LARSSON, A; WICTORIN, L ; JOENSSON, S E

PRIORITY-DATA: 1994SE-0001558 (May 5, 1994)

### PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9530402 A1	November 16, 1995	E	019	A61K006/087
DE 69519038 E	November 9, 2000		000	A61K006/087
SE 9401558 A	November 6, 1995		000	A61K006/087
AU 9524591 A	November 29, 1995		000	A61K006/087
SE 502812 C2	January 22, 1996		000	A61K006/087
EP 788344 A1	August 13, 1997	E	000	A61K006/087
EP 788344 B1	•	E	000	A61K006/087
<u> </u>	•			

INT-CL (IPC):  $A61 \times 6/087$ 

ABSTRACTED-PUB-NO: EP 788344B

BASIC-ABSTRACT:

A photopolymerisable dental filling compsn. is based on monomers of formula (I), esp. 3,4-epoxycyclohexyl-methyl-3,4-epoxy-cyclohexane-carbox- ylate (IA) or bis-(3,4-epoxycyclohexyl)-adipate (IB) A,B and C = 0-10 (pref. 0-2) atom chain; X = -0-, -NH.CO-, -NH-, -CO- or a chemical band; and Y1 and Y2 = opt. substd. carboxylic, heterocyclic, aliphatic or aromatic ring of 5,6 or 7 ring atoms.

ADVANTAGE - The compsns. show low shrinkage (eg. 0.08-0.17 linear %) on curing with UV or visible light, white (I) show low index values in skin irritation tests (eg. 0.5 in a 0-8 index scale).

ABSTRACTED-PUB-NO:

## WO 9530402A EQUIVALENT-ABSTRACTS:

A photopolymerisable dental filling compsn. is based on monomers of formula (I), esp. 3,4-epoxycyclohexyl-methyl-3,4-epoxy-cyclohexane-carbox- ylate (IA) or bis-(3,4-epoxycyclohexyl)-adipate (IB) A,B and C = 0-10 (pref. 0-2) atom chain; X = -O-, -NH.CO-, -NH-, -CO- or a chemical band; and Y1 and Y2 = opt. substd. carboxylic, heterocyclic, aliphatic or aromatic ring of 5, 6 or 7 ring atoms.

ADVANTAGE - The compsns. show low shrinkage (eg. 0.08-0.17 linear %) on curing with UV or visible light, white (I) show low index values in skin irritation tests (eg. 0.5 in a 0-8 index scale).

☐ 5. Document ID: SE 8002785 A

L15: Entry 5 of 6

File: DWPI

Nov 16, 1981

DERWENT-ACC-NO: 1982-11178E

DERWENT-WEEK: 198206

COPYRIGHT 2004 DERWENT INFORMATION LTD

TITLE: Gold alloy for use in dental technology - contains cobalt and opt. chromium

and molybdenum

INVENTOR: FREDRIKSSO, H; WICTORIN, L

PRIORITY-DATA: 1980SE-0002785 (April 14, 1980)

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

SE 8002785 A

November 16, 1981

003

INT-CL (IPC): C22C 5/02

ABSTRACTED-PUB-NO: SE 8002785A

BASIC-ABSTRACT:

Dental alloy comprises 90 wt.% gold and 10 wt.% cobalt. The alloy can be heat treated to various hardness es. to approx. 200 Hv, and the presence of only two elements prevents inhomogeneous structure and corrosion.

A second dental alloy comprises 75-80 wt.% gold 0-10wt.% Cobalt, 0-10% chromium, and/or 0-5 wt.% Molybdenum and 0-5 wt.% Palladium, to which a porcelain layer can be fired. The alloy heat treatment comprises a soln. stage at 850-930 deg.C followed by hardening at 100-400 deg.C and rapid cooling. (Provisional Basic previously advised in Week D49).

Full Title	e Citation Front Review Classification D	ate Reference		Claims	Killin	Draws Desc
				-		
		***************************************	 			
□ 6.	Document ID: US 3752654 A					

L15: Entry 6 of 6

File: USOC

Aug 14, 1973

US-PAT-NO: 3752654

DOCUMENT-IDENTIFIER: US 3752654 A

TITLE: ABSORPTION UNIT FOR THE ABSORPTION OF CARBON DIOXIDE

DATE-ISSUED: August 14, 1973

US-CL-CURRENT: 422/120; 128/205.28, 96/118

DOCUMENT TEXT:

Aug. 14, 1973 31752,6540 D. O. A. JOHANNISSON ET AL ABSORPTIO"Q UNIT FOR THE ABSORPTION OF CARBON I) IOXIDE Filed Feb. 10; 1972 4- FIG.1 4 FIG. A? FIG.,5 10 "'I 4" 15 15

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.16&ref=15&dbname=PGPB,USPT,U... 10/27/04

3 1 7 5 2 @ 6 5 4 Utiited States Patent Office' Patented Aug. 14, 1973 3,752,654 ABSORPIION UNIT FOR THE ABSORPTION OF CARBON DIOXIDE Dag 0. A. Johannisson and Ake G. R. Wictorin, Lidingo, Sweden, assignors to Aga Aktiebolag, Lidingo, Sweden 5 Filed Feb. 10, 1972, Ser. No. 225,035 Claims priority, application Sweden, Feb. 15, 1971, 1,859/71 Int. Cl. Bold 53104, B01i 1114, A62b 7110 U.S. Cl. 23-284 6 Claims 10 ABSTRACT OF THE DISCLOSURE In an absorption unit for the absorption of carbon dioxide, especially for a breathing apparatus having a sub- 15 stantiahy closed gas system the space inside the unit is divided in a plurality of chambers, each one of which is filled with a carbon dioxide absorbing substance and bounded by walls of a porous material permitting the gas to pass from an inlet of the unit, through the walls and 20 the substance to an outlet of the unit. FIELD, OF THE INVENTION The present invention refers to an absorption unit for 25 the absorption of carbon dioxide of the kind which pref- erably can be used in a breathing apparatus having a sub- stantially closed gas system. BACKGROUND OF THE INVENTION 30 In a breathing apparatus having a substantially closed gas system breathing gas is caused to circulate while car- bon dioxide is absorbed and oxygen added so that the oxygen which is supplied to a patient is compensated for. An absorption unit for that purpose comprises a cor, tainer 35 with an inlet and an outlet and holding a substance adapted f6r absorbing carbon dioxide. PRIOR ART 40 -In prior absorption units which have comprised a con-tainer, the entire interior of which has been filled with the carbon dioxide absorbing substance it has been pos- sible to obtain a tiine of use in the order of 2 hours, which means that after this time the carbon dioxide has been 45 able to pass through the absorption unit without being absorbed. Then the total amoiint of the carbon dioxide absorbing substance has not been consumed but the passage of carbon dioxide through the absorption unit has been enabled since the carbon dioxide absorbing properties 50 of this substance has been used up within certain chan- nels or passages inside the substance. SUMMA.RY OF THE INVENTION According to the present invention a much better exploi- 55 tation of the carbon dioxide absorbing substance can be achieved in the same time as only a smaller amount of this substance is needed. This result has been achieved in that the space inside the container is divided into a plurality of chambers, each one of which is filled with the carbon di-60 oxide absorbing substance and in all directions bounded by partitions made of a porous material, such as poly- ether foamed plastic. BRIEF DESCRIPTION OF, TH-E DRAWING 65 'fhe invention is described below with reference to the annexed drawing, in which FIG. I schematically shows a breathing apparatus with an absorption unit according to the invention, FIG. 2 shows a section of the abs6rption 70 2 unit and FIG. 3 shows a section perpendicular to the sec- tion of FIG. 2. DESCRIPTION OF THE PREFERRED EMBODIMENT The absorption unit is made of @a container I which is connected with a tube 4 leading to a patient over a breathmg in tube 2 and a breathing out tube 3. In the closed gas system which is formed by the container I and the tubes 2 and 3 chec@k valves 5 and 6 are inserte(I for controlling the direction of the gasffow inside the gas system. A conduit 7 for supplying fresh breathing gas intended for compensating for oxygen which has been used up by the patient is connected with the breathing in tube 2 and this conduit 7 is provided with a chec@k valve 8. Finally the gas system comprises a breathing bag 9 having variable volume, for instance a rubber bag which is connected with the inlet of the absorption unit 1. From FIGS. 2 and 3 it is seen that the absorption unit 1 within a cylin&ical outer wall 10 which is connected with a bottom 1,1 and closed by a lid 12 comprises a plurality of sector formed chambers 13, in this case twelve ambers, which surround a central, cylindricary formed amber 14. These chambers are bounded in all directions by partitions 15 of a porous material which preferably consists of polyether foamed plastic. Thus, the partitions form an outer annular part, an inner annular part and between these a plurality of radially directed partitions, in this case twelve partitions. FIG. 3 indicates that the porous material 15 also can form the bottom and the lid of the chambers 13 and 14, but it is also possible that the bottom 11 and the lid 12 of the container I may lie directly and sealingly against the outer annular part, the inner annular part and the radially directed partitions of the porous material. By this configuration of the absorption unit the result is obtained that it comprises a much smaller amount of the carbon dioxide absorbing substance compared with the prior absorption units. While the prior absorption units had to be filled with about 600 gr. of the carbon dioxide absorbing substance the unit according to the invention needs only about 450 gr. In spite of this the time of use has been

expanded from about 2 hours with the prior unit to about 31/2 hours with the unit according to the invention. Thus, a substantial improvement has been obtained in these two regards, and furthermore, the partitions of the porous material contributes to hold any dust emanating from the carbon dioxide absorbing substance. This substance may be of the type called "sodasorb" and consists of a granulate of sodiumhy&oxide-caustic potash. Preferably, the lid 12 is fastened to the cylindrical wall of the container so that a certain compression of the porous mate al in the partitions 15 is obtained, whereby a sufficient sealing is achieved between this porous material and the cylindrical wall and the plane bottom and lid of the container. Thereupon, the lid can be joined to the cylindrical wall by glueing since a used unit normally is disposed with and replaced by a fresh unit. It is claimed: 1. Absorption unit for the absorption of carbon dioxide, especially for a breathing apparatus having a substantially closed gas system, in which breathing gas is caused to circulate while carbon dioxide is absorbed and oxygen is added, comprising a container having an inlet and an outlet and holding a carbon dioxide absorbing substance, characterized in that the carbon dioxide absorbing substance is placed in a Plurality of chambers (13, 14) in the container (1, 10, 11, 12) which are separated from each other, whereas each chamber is bounded by partitions

3.752,654 (15) -of a -porous material which allows the gas to pass from the inlet, through the partitions and the- carbon dioxide absorbing substance to the outlet. 2. Absorption unit as claimed in claim I in which the partitions (15) are made of polyether foamed plastic. 1 3.: Absorption unit as claimed in claim 1, in which the container has a circular outer wall (10) and substantially plane bottom (11) and a plane lid (12). 4. Absorption unit as claimed in claims 2 and 3, in which the lid (12) is sealifigly fa8tened to the cylindrical outer wall (10) qnder compression of the porous material of the partitions (15). Absorptio . n unit@ as claimed in claim 3, in which the container is provided with a plurality of sector formed chambers (13) surrounding a central, cylindrically formed chamber (14). 6. Absorption unit as claimed in claim 3, in which the inlet and the outlet of the abgorption unit are arranged in the cylindrical outer wall of the container and diametrically with regard to each other.. 5 References Cited UNITED STATES PATENTS 3,464,186 9/1969 - Hankison et al - ----- 55-387 10 3,5166,867 3/1971 Dryden ----- 128-188 31615,233 10/1971 Dbening ----- -- 23-252 CHARLES N. HART, Primary Examiner U.S. Cl. X@R. 15 23-252; 55-387; 128-142.6

Full   Title   Citation	Front Review	Classification	Date	Reference			C	laims	KWMC	Draw, Des
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# **Hit List**

Clear Generate Collection Print Fwd Refs Bkwd Refs Generate OACS

Search Results - Record(s) 1 through 93 of 93 returned.

☐ 1. Document ID: US 20040161419 A1

Using default format because multiple data bases are involved.

L21: Entry 1 of 93

File: PGPB

Aug 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040161419

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040161419 A1

TITLE: Placental stem cells and uses thereof

PUBLICATION-DATE: August 19, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Strom, Stephen C.

Allison Park

PΑ

US

Miki, Toshio

Pittsburgh

PΑ

US

US-CL-CURRENT: 424/93.21; 435/366

Full Title Citation Fr	ront Review Clas	sification Date	Reference	Sequences	Attachments	Claims	KMC	Draw, Desc

☐ 2. Document ID: US 20040152189 A1

L21: Entry 2 of 93

File: PGPB

Aug 5, 2004

PGPUB-DOCUMENT-NUMBER: 20040152189

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040152189 A1

TITLE: Selective antibody targeting of undifferentiated stem cells

PUBLICATION-DATE: August 5, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

McWhir, Jim

Midlothian

CA

GB

Gold, Joseph D.

San Francisco

CA

US

Schiff, J. Michael

Menlo Park

US

US-CL-CURRENT: 435/366; 435/455

ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U... 10/27/04

cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in expression of a cell-surface antigen that can be used to deplete the undifferentiated cells. Model effector sequences encode glycosyl transferases that synthesize carbohydrate xenoantigen or alloantigen, which can be used for immunoseparation or as a target for complement-mediated lysis. The differentiated cell populations produced are suitable for use in tissue regeneration and non-therapeutic applications such as drug screening.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims RMC Draw Description 3. Document ID: US 20040137535 A1

L21: Entry 3 of 93

File: PGPB

Jul 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040137535

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040137535 A1

TITLE: Enriched central nervous system stem cell and progenitor cell populations, and

methods for identifying, isolating and enriching for such populations

PUBLICATION-DATE: July 15, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Uchida, Nobuko Palo Alto CA US Capela, Alexandra Mountain View CA US

US-CL-CURRENT: 435/7.2; 435/368

### ABSTRACT:

Enriched neural stem and progenitor cell populations, and methods for identifying, isolating and enriching for neural stem cells using reagents that bind to cell surface markers are provided.

Full	Title Citation Front	Review Classification [	ate Reference	Sequences	Attachments	Claims	KWIC	Draw Desc
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	4. Document ID:	US 20040121460 A	<b>1</b>					
721.	Entry 4 of 93		File: F	GPB		Jun	24,	2004

PGPUB-DOCUMENT-NUMBER: 20040121460

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040121460 A1

TITLE: Differentiation of stem cells to pancreatic endocrine cells

PUBLICATION-DATE: June 24, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lumelsky, Nadya L	Washington	DC	US	
Blondel, Oliver	Bethesda	MD	US	
McKay, Ronald D	Bethesda	MD	US	
Kim, Jong-Hoon	Rockville	MD	US	

US-CL-CURRENT: 435/366; 435/354

#### ABSTRACT:

A method is provided for differentiating embryonic stem cells to endocrine cells. The method includes generating embryoid bodies from a culture of undifferentiated embryonic stem cells, selecting endocrine precursor cells, expanding the endocrine precursor cells by culturing endocrine cells in an expansion medium that comprises a growth factor, and differentiating the expanded endocrine precursor cells in a differentiation media to differentiated endocrine cells produced by this method are also provided. Artificial islets are disclosed, as well as method for using the pancreatic endocrine cells and the artificial islets.

Full Title Citation Front Review Classification Date	e Reference Sequences Attachmi	ents Claims KMC Draw. Desi
☐ 5. Document ID: US 20040121380 A1		
L21: Entry 5 of 93	File: PGPB	Jun 24, 2004

PGPUB-DOCUMENT-NUMBER: 20040121380

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040121380 A1

TITLE: Novel polypeptides and nucleic acids encoding same

PUBLICATION-DATE: June 24, 2004

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Taupier, Raymond J. JR.	East Haven	CT	US	
Majumder, Kumud	Stamford	CT	US ·	
Spaderna, Steven K.	Berlin	CT	US	
Smithson, Glennda	Guilford	CT	US	
Mezes, Peter S.	Old Lyme	CT	US	
Vernet, Corine A.M.	North Branford	CT	US	

US-CL-CURRENT:  $\underline{435/6}$ ;  $\underline{435/320.1}$ ,  $\underline{435/325}$ ,  $\underline{435/69.1}$ ,  $\underline{530/350}$ ,  $\underline{530/388.1}$ ,  $\underline{536/23.2}$ 

### ABSTRACT:

The present invention provides novel isolated NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any derivative, variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to other uses.

## ☐ 6. Document ID: US 20040107453 A1

L21: Entry 6 of 93

File: PGPB

Jun 3, 2004

PGPUB-DOCUMENT-NUMBER: 20040107453

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040107453 A1

TITLE: Multipotent adult stem cells, sources thereof, methods of obtaining same, methods of differentiation thereof, methods of use thereof and cells derived thereof

PUBLICATION-DATE: June 3, 2004

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Furcht, Leo T	Minneapolis	MN	US	
Verfaillie, catherine M	St Paul	MN	US	
Reyes, Morayma	Minneapolis	MN	US	

US-CL-CURRENT: 800/18; 424/93.7, 435/353, 435/354, 435/366, 800/21

### ABSTRACT:

The present invention relates generally to mammalian multipotent adult stem cells (MASC), and more specifically to methods for obtaining, maintaining and differentiating MASC to cells of multiple tissue types. Uses of MASC in the therapeutic treatment of disease are also provided.

Full	Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC	Drawt Des
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1. Document ID: US 20040096828 A1

L21: Entry 7 of 93

File: PGPB

May 20, 2004

PGPUB-DOCUMENT-NUMBER: 20040096828

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040096828 A1

TITLE: Cytoskeleton-associated proteins

PUBLICATION-DATE: May 20, 2004

## INVENTOR-INFORMATION:

CITY	STATE	COUNTRY	RULE-47
San Jose	CA	US	
San Leandro	CA	US	
Mountain View	CA	US	
San Carlos	CA	US ·	
Sunnyvale	CA	US	
	San Jose San Leandro Mountain View San Carlos	San Jose CA San Leandro CA Mountain View CA San Carlos CA	San Jose CA US San Leandro CA US Mountain View CA US San Carlos CA US

Tang, Y Tom	San Jose	CA	US
Warren, Bridget A	San Marcos	CA	US
Duggan, Brendan M	Sunnyvale	CA	US
Xu, Yuming	Mountain View	CA	US
Chawla, Narinder K	Union City	CA	US
Griffin, Jennifer A	Fremont	CA	US
Stewart, Elizabeth A	Mill Creek	AW	US
Gandhi, Ameena R	San Francisco	CA	US
Khan, Farrah A	Des Plaines	IL	US.
Thangavelu, Kavitha	Sunnyvale	CA	US
Ison, Craig H	San Jose	CA	US
Azimzai, Yalda	Oakland	CA	US
Hafalia, April J A	Daly City	CA	US
Gietzen, Kimberly J	San Jose	CA	US
Lal, Preeti G	Santa Clara	CA	US
Madhusudan, Sanjanwala M	Los Altos	CA	US
Elliott, Vicki S	San Jose	CA	US

US-CL-CURRENT:  $\underline{435/6}$ ;  $\underline{435/320.1}$ ,  $\underline{435/325}$ ,  $\underline{435/69.1}$ ,  $\underline{530/350}$ ,  $\underline{530/388.1}$ ,  $\underline{800/18}$ 

#### ABSTRACT:

The invention provides <u>human</u> cytoskeleton-associated proteins (CSAP) and polynucleotides which identify and encode CSAP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with aberrant expression of CSAP.

Full Title Citation Front Review Classification Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desi
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☐ 8. Document ID: US 20040092013 A1					•	
L21: Entry 8 of 93	File:	PGPB		Мау	13,	2004

PGPUB-DOCUMENT-NUMBER: 20040092013

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040092013 A1

TITLE: Method of treating alzheimer's disease with cell therapy

PUBLICATION-DATE: May 13, 2004

### INVENTOR-INFORMATION:

CITY	STATE	COUNTRY	RULE-47
La Jolla	CA	US	
Del Mar	CA	US	
Atherton	CA	US	
Arcadia	CA	US	
Palo Alto	CA	US	
	La Jolla Del Mar Atherton Arcadia	La Jolla CA Del Mar CA Atherton CA Arcadia CA	La Jolla CA US Del Mar CA US Atherton CA US Arcadia CA US

US-CL-CURRENT: 435/368; 424/93.7

### ABSTRACT:

A method of treating Alzheimer's disease provides for administering NSC to a susceptible individual. Preferably the NSCs are administered intracisternally. Other administration routes are spinal injection, ventricular injection or systemic injection. Preferably, the quantity of NSC administered is in a range of about 400,000 to about 40,000,000. More preferably, the quantity of NSC is about 1,000,000 to about 10,000,000. The NSCs are administered at multiple locations. The NSCs can be administered to the neocortex or other affected areas of both hemispheres. The method of preventing further deterioration in cognitive function in a person diagnosed with Alzheimer's disease provides for administering NSC to the person in sufficient quantity to prevent additional loss of cognitive function.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims	KMMC   Draw, Desi
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☐ 9. Document ID: US 20040072344 A1			
L21: Entry 9 of 93	File: PGPB	Aŗ	or 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040072344

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040072344 A1

TITLE: Method for inducing differentiation of embryonic stem cells into functioning cells

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Inoue, Kazutomo	Kyoto-shi		JP	
Kim, Dohoon	Kyoto-shi		JP	
Gu, Yanjun	Kyoto-shi		JP	
Ishii, Michiyo	Kyoto-shi		JP	

US-CL-CURRENT: <u>435/366</u>

### ABSTRACT:

The present invention provides a 4-step method for inducing differentiation of embryonic stem cells into functioning cells comprising 1) expanding ES cells; 2) inducing Embryoid Bodies in the presence of leukemia inhibitory factor and basic FGF; 3) selection expanding of the EBs and 4) differentiation. According to the present invention, ES cells can be differentiated into either insulin producing pancreatic islet like cell clusters or nerve like cells. Thus obtained functioning cells may be potential sources of donor cells in cell transplant therapy for many patients.

Full Title Citation Front Review Classificatio	n Date Reference Sequences Atta	achments   Claims   KWIC   Draw. Des
magaaanaanaanaanaanaanaanaanaanaanaanaana		
☐ 10. Document ID: US 200400588	362 A1	
L21: Entry 10 of 93	File: PGPB	Mar 25, 2004

PGPUB-DOCUMENT-NUMBER: 20040058862

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040058862 A1

TITLE: Novel polypeptides and nucleic acids encoding the same

PUBLICATION-DATE: March 25, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Majumder, Kumud Stamford CT US

US-CL-CURRENT: 514/12; 424/130.1, 435/320.1, 435/325, 435/69.1, 435/7.1, 530/350,

530/388.1, 536/23.5

### ABSTRACT:

The present invention provides novel isolated NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any derivative, variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to other uses.

Full Title	Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Desc
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□ 11.	Document ID: US 20040033597 A1

File: PGPB

Feb 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040033597

PGPUB-FILING-TYPE: new

L21: Entry 11 of 93

DOCUMENT-IDENTIFIER: US 20040033597 A1

TITLE: Multipotent neural stemcells from peripheral tissues and uses thereof

PUBLICATION-DATE: February 19, 2004

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Toronto Ontario		CA	
Akhavan, Mahnaz	Toronto Ontario		CA	
Fernandes, Karl J. L.	Toronto Ontario		CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Toronto Ontario		CA	
Golster, Andrew	Saskatoon Sakatchewan		CA	

US-CL-CURRENT: 435/368; 435/371

### ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KWIC Draw Desc

☐ 12. Document ID: US 20040009593 A1

L21: Entry 12 of 93

File: PGPB

Jan 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040009593

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040009593 A1

TITLE: Oligodendrocytes derived from human embryonic stem cells for remyelination and

treatment of spinal cord injury

PUBLICATION-DATE: January 15, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Keirstead, Hans S.

Irvine

CA

US

Nistor, Gabriel I.

Placentia

CA

US

US-CL-CURRENT: 435/368

## ABSTRACT:

This invention provides populations of neural cells bearing markers of glial cells, such as oligodendrocytes and their precursors. The populations are generated by differentiating pluripotent stem cells such as <a href="https://www.nummar.n

Full Title Citation	Front Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWAC	Drawi Desc
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☐ 13. Document ID: US 20030216308 A1

L21: Entry 13 of 93

File: PGPB

Nov 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030216308

PUBLICATION-DATE: November 20, 2003

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030216308 A1

TITLE: Novel polypeptides and nucleic acids encoding same

•

INVENTOR-INFORMATION:

NAME

CITY

STATE COUNTRY

RULE-47

Anderson, David W.

Branford

CT

US

Guo, Xiaojia (Sasha)	Branford	CT	US
Gusev, Vladimir Y.	Madison	CT	US
Herrmann, John L.	Guilford	CT	US
Li, Li	Branford	CT .	US
Mezes, Peter S.	Old Lyme	CT	US
Padigaru, Muralidhara	Branford	CT	US
Patturajan, Meera	Branford	CT	US
Pena, Carol E. A.	New Haven	CT	US
Rastelli, Luca	Guilford	CT	US
Shimkets, Richard A.	Guilford	CT	US
Smithson, Glennda	Guilford	CT	US
Spaderna, Steven K.	Berlin	CT	US
Taupier, Raymond J. JR.	East Haven	CT	US
Vernet, Corine A.M.	Branford	CT	US

US-CL-CURRENT: 514/12; 435/320.1, 435/325, 435/6, 435/69.1, 530/350, 536/23.5

## ABSTRACT:

The present invention provides novel isolated NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any derivative, variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to other uses.

Full Title Citation Front Review Classification	Date Reference Sequences Atta	chments   Claims   KWC   Draw. Desc
	***************************************	·······
☐ 14. Document ID: US 2003021160	03 A1	
L21: Entry 14 of 93	File: PGPB	Nov 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030211603

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030211603 A1

TITLE: Reprogramming cells for enhanced differentiation capacity using pluripotent stem cells

PUBLICATION-DATE: November 13, 2003

# INVENTOR-INFORMATION:

THAPPAIOU THE OPERATOR				
NAME	CITY	STATE	COUNTRY	RULE-47
Earp, David J.	Oakland	CA	US	
Carpenter, Melissa K.	Castro Valley	CA	US	
Gold, Joseph D.	San Francisco	CA	US	
Lebkowski, Jane S.	Portola Valley	CA	US	
Schiff, J. Michael	Menlo Park	CA	US	

US-CL-CURRENT: <u>435/366</u>

#### ABSTRACT:

Described in this disclosure is a new process whereby cells of one tissue type can be reprogrammed to produce cells of a different tissue type. Cells from a <a href="https://www.numman

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims	KWMC   Draw Desc
☐ 15. Document ID: US 20030207450 A1			
L21: Entry 15 of 93	File: PGPB	No	ov 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030207450

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030207450 A1

TITLE: Isolation and transplantation of retinal stem cells

PUBLICATION-DATE: November 6, 2003

INVENTOR-INFORMATION:

RULE-47 · COUNTRY CITY STATE NAME US Young, Michael J. Gloucester US CA Pasadena Klassen, Henry J. US Athol MA Shatos, Marie A. Mizumoto, Keiko Higashi JΡ

US-CL-CURRENT: 435/368

# ABSTRACT:

The present invention relates to the isolation, in vitro propagation, and transplantation and integration of non-pigmented retinal stem cells derived from the neuroretina of the eye, ex vivo and in vivo.

Full Title Citation Front Review	Classification Date	Reference	Sequences	Attachments	Claims	KWAC	Draw Desc
	0000175054 A 1						
☐ 16. Document ID: US 20	1030173934 AT						
L21: Entry 16 of 93		File:	PGPB		Sep	18,	2003

PGPUB-DOCUMENT-NUMBER: 20030175954

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175954 A1

TITLE: Human embryoid body-derived cells

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Shamblott, Michael J.

Baltimore

MD

US

Gearhart, John D.

Baltimore

MD

US

US-CL-CURRENT: 435/366; 435/69.1

#### ABSTRACT:

The invention is directed to novel cells that are derived from human embryoid bodies. Such embryoid body-derived (EBD) cells are relatively uncommitted or progenitor (e.g., pluripotent) cells. EBD cells, while not immortal, display long-term proliferation in culture with a normal karyotype and can be cryopreserved and cloned. They can be efficiently transfected with retroviruses and lentivirus and genetically manipulated. Although they have a developmentally broad multilineage expression profile, they do not form tumors when injected into severe combined immunodeficiency (SCID) mice. As a result, EBD cells have a variety of uses, for example, in transplantation therapies.

Full Title Citation Front Review Classification (	Date Reference	Sequences	Attachments Claims	KMC Draw Desc
		······································	······································	<i></i>
☐ 17. Document ID: US 20030170736	Al		·	
L21: Entry 17 of 93	File:	PGPB	Seg	o 11, 2003

PGPUB-DOCUMENT-NUMBER: 20030170736

PGPUB-FILING-TYPE: new

L21: Entry 17 of 93

DOCUMENT-IDENTIFIER: US 20030170736 A1

TITLE: Methods and compositions for producing neural progenitor cells

PUBLICATION-DATE: September 11, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

RULE-47

Agoston, Denes V.

Bethesda

MD

US

COUNTRY

US-CL-CURRENT: 435/7.2; 435/368, 435/455, 530/388.26

#### ABSTRACT:

The invention relates generally to methods and compositions for altering the differentiation status of cells such as stem and progenitor cells, and producing these cells for transplantation into mammals. The differentiation status of cells can be altered by contacting a nucleic acid decoy molecule to a mammalian cells and culturing the cell, whereby the differentiation status of the cell is altered. Pharmaceutical compositions of the invention are capable of entering a cell and binding to a protein in the cell and thereby altering a septamer function, a septamer-downstream function or a septamer-related function. The methods disclosed herein can be used in treating diseases by providing new cells to ameliorate symptoms of the disorder. Preferably, methods of the invention create homogeneous populations of progenitor and other cells, that can be administered to patients by transplantation. Diseases and disorders that can be treated in this fashion include, but are not limited to, CNS disorders, disorders of the lymphatic system, endothelial cell disorders, epithelial cell disorders, erythropoietic and hematopoietic diseases and disorders, neuro-degenerative disease, and traumatic brain injuries.

# ☐ 18. Document ID: US 20030166272 A1

L21: Entry 18 of 93

File: PGPB

Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166272

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030166272 A1

TITLE: Method of preparing an undifferentiated cell

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Abuljadayel, Ilham Saleh

London

GB

US-CL-CURRENT: 435/366

#### ABSTRACT:

A method of increasing the relative number of cells expressing one or more stem cell markers in a cell population including committed cells is described. The method comprises: i. contacting the cell population with an agent that operably engages said committed cells; and ii. incubating committed cells that are engaged by said agent such that the relative number of cells expressing one or more stem cell markers increases as a result of said engaging.

Full		Review   Classification					Draw, Des
	19. Document ID:		•				
L21:	Entry 19 of 93		File:	PGPB	Aug	28,	2003

PGPUB-DOCUMENT-NUMBER: 20030162290

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162290 A1

TITLE: Method for inducing differentiation of embryonic stem cells into functioning cells

PUBLICATION-DATE: August 28, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Inoue, Kazutomo	Sakyo-ku		JР	
Kim, Dohoon	Sakyo-ku		JP	
Gu, Yanjun	Sakyo-ku		JP	
Ishii, Michiyo	Kamigyo-ku		JP	

US-CL-CURRENT: 435/366; 435/372

## ABSTRACT:

The present invention provides a 4-step method for inducing differentiation of embryonic stem cells into functioning cells comprising 1) expanding ES cells; 2) inducing Embryoid Bodies in the presence of leukemia Inhibitor factor and basic FGF; 3) selection expanding of the EBs and 4) differentiation. According to the present invention, ES cells can be differentiated into either insulin producing pancreatic islet like cell clusters or nerve like cells. Thus obtained functioning cells may be potential sources of donor cells in cell transplant therapy for many patients.

Full Title Citation Front Review Classification Date	Reference   Sequences	Attachments Claim	ns   KWWC   Draww Desc
☐ 20. Document ID: US 20030161817 A1 L21: Entry 20 of 93	File: PGPB	Į	Aug 28, 2003

PGPUB-DOCUMENT-NUMBER: 20030161817

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030161817 A1

TITLE: Pluripotent embryonic-like stem cells, compositions, methods and uses thereof

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Young, Henry E. Macon GA US
Lucas, Paul A. Poughkeepsie NY US

US-CL-CURRENT: 424/93.21; 435/366

L21: Entry 21 of 93

### ABSTRACT:

The present invention relates to pluripotent stem cells, particularly to pluripotent embryonic-like stem cells. The invention further relates to methods of purifying pluripotent embryonic-like stem cells and to compositions, cultures and clones thereof. The present invention also relates to a method of transplanting the pluripotent stem cells of the present invention in a mammalian host, such as <a href="https://www.numman.comprising">https://www.numman.comprising</a> introducing the stem cells, into the host. The invention further relates to methods of in vivo administration of a protein or gene of interest comprising transfecting a pluripotent stem cell with a construct comprising DNA which encodes a protein of interest and then introducing the stem cell into the host where the protein or gene of interest is expressed. The present also relates to methods of producing mesodermal, endodermal or ectodermal lineage-committed cells by culturing or transplantation of the pluripotent stem cells of the present invention.

	Full   Title	Citation   Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desi
•••••							·····			<b></b>	<del></del>
	□ 21.	Document ID	: US 2	003014848	5 A1						

File: PGPB

Aug 7, 2003

PGPUB-DOCUMENT-NUMBER: 20030148485

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030148485 A1

TITLE: Novel polypeptides and nucleic acids encoding same

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

<b>2217 221</b> 221 221 221				
NAME	CITY	STATE	COUNTRY	RULE-47
Taupier, Raymond J. JR.	East Haven	CT	US	
Majumder, Kumud	Stamford	CT	US	
Spaderna, Steven K.	Berlin	CT	US	
Smithson, Glennda	Guilford	CT	US	
Mezes, Peter S.	Old Lyme	CT	US	
Vernet, Corine A.M.	North Branford	CT	US	

US-CL-CURRENT:  $\underline{435/189}$ ;  $\underline{435/320.1}$ ,  $\underline{435/325}$ ,  $\underline{435/6}$ ,  $\underline{435/69.1}$ ,  $\underline{536/23.2}$ 

## ABSTRACT:

The present invention provides novel isolated NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any derivative, variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention additionally provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, as well as to other uses.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims KWC Draw Desc
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☐ 22. Document ID: US 20030134413 A1		
L21: Entry 22 of 93	File: PGPB	Jul 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030134413

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030134413 A1

TITLE: Cell production

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Rathien, Peter David Mircham AU

Rathjen, Peter David Mircham AU
Rathjen, Joy Mircham AU

US-CL-CURRENT: 435/368

# ABSTRACT:

A method of producing neurectoderm cells, which method includes providing a source of early primitive ectoderm-like (EPL) cells; a conditioned medium as hereinbefore

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U... 10/27/04

defined; or an extract therefrom exhibiting neural inducing properties; and contacting the EPL cells with the conditioned medium, for a time sufficient to generate controlled differentiation to neurectoderm cells.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KWC Draw. Desc

☐ 23. Document ID: US 20030118566 A1

L21: Entry 23 of 93

File: PGPB

Jun 26, 2003

PGPUB-DOCUMENT-NUMBER: 20030118566

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030118566 A1

TITLE: Compositions and methods for isolation, propagation, and differentiation of

human stem cells and uses thereof

PUBLICATION-DATE: June 26, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Neuman, Toomas

Santa Monica

CA

US

Levesque, Michel

Beverly Hills

CA

US

US-CL-CURRENT: 424/93.21; 424/93.7, 435/368

## ABSTRACT:

The invention is directed to the field of  $\underline{\text{human}}$  stem cells and includes methods and compositions for isolating, propagating, and differentiating  $\underline{\text{human}}$  stem cells. The invention provides therapeutic uses of the methods and compositions, including autologous transplantation of treated cells into  $\underline{\text{humans}}$  for treatment of Parkinson's and other neuronal disorders.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw. De	····
[4] Mie Platon   John   Manero   Signature   Manero   Man	Ş1
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# ☐ 24. Document ID: US 20030113910 A1

L21: Entry 24 of 93

File: PGPB

Jun 19, 2003

PGPUB-DOCUMENT-NUMBER: 20030113910

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030113910 A1

TITLE: Pluripotent stem cells derived without the use of embryos or fetal tissue

PUBLICATION-DATE: June 19, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Levanduski, Mike

River Vale

NJ

US

US-CL-CURRENT: 435/325; 435/354, 435/366

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U... 10/27/04

# ABSTRACT:

This invention provides a method for deriving precursors to pluripotent non-embryonic stem (P-PNES) and pluripotent non-embryonic stem (PNES) cell lines. The present invention involves nuclear transfer of genetic material from a somatic cell into an enucleated, zona pellucida free <a href="human">human</a> ooplastoid having a reduced amount of total cytoplasm. The present invention provides a new source for obtaining human and other animal pluripotent stem cells. The source utilizes as starting materials an oocyte and a somatic cell as the starting materials but does not require the use, creation and/or destruction of embryos or fetal tissue and does not in any way involve creating a cloned being. The oocyte never becomes fertilized and never develops into an embryo. Rather, portions of the oocyte cytoplasm are extracted and combined with the nuclear material of individual mature somatic cells in a manner that precludes embryo formation. Murine, bovine, and human examples of the procedure are demonstrated. Subsequently, the newly constructed P-PNES cells are cultured in vitro and give rise to PNES cells and cell colonies. Methods are described for culturing the P-PNES cells to yield purified PNES cells which have the ability to differentiate into cells derived from mesoderm, endoderm, and ectoderm germ layers. Methods are described for maintaining and proliferating PNES cells in culture in an undifferentiated state. Methods and results are described for analysis and validation of pluripotency of PNES cells including cell morphology, cell surface markers, pluripotent tumor development in SCID mouse, karyotyping, immortality in in vitro culture.

Full	Title	Citation Front R	eview	Classification	Date	Reference	Sequences	Attachments	Claims	KWWC   Draw, Desc
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	25.	Document ID:	US 20	003010904	1 A1					

File: PGPB

PGPUB-DOCUMENT-NUMBER: 20030109041

PGPUB-FILING-TYPE: new

L21: Entry 25 of 93

DOCUMENT-IDENTIFIER: US 20030109041 A1

TITLE: Lineage restricted glial precursors from the central nervous system

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

STATE RULE-47 COUNTRY NAME CITY US Salt Lake City UT Rao, Mahendra S. NY US Brighton Noble, Mark NY US Mayer-Proschel, Margot Pittsford

US-CL-CURRENT: 435/368

## ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

Jun 12, 2003

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KWIC

☐ 26. Document ID: US 20030103949 A1

L21: Entry 26 of 93

File: PGPB

Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030103949

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030103949 A1

TITLE: Screening small molecule drugs using neural cells differentiated from human

embryonic stem cells

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	
Denham, Jerrod J.	San Francisco	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Thies, R. Scott	Pleasanton	CA	US	

US-CL-CURRENT: 424/93.21; 435/368, 435/4

### ABSTRACT:

This invention provides populations of neural progenitor cells and differentiated neurons, obtained by culturing pluripotent cells in special growth cocktails. The technology can be used to produce progenitors that proliferate through at least .about.40 doublings, while maintaining the ability to differentiate into a variety of different neural phenotypes, including dopaminergic neurons. The neural progenitors and terminally differentiated neurons of this invention can be generated in large quantities for use in drug screening and the treatment of neurological disorders.

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Full Title Citation	Front Review Classification	Date Reference	Sequences	Attachments C	laims KMC	Draw, Des
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☐ 27. Docum	ment ID: US 20030082152	Al				
L21: Entry 27 o	of 93	File:	PGPB		May $1$ ,	2003

PGPUB-DOCUMENT-NUMBER: 20030082152

PGPUB-FILING-TYPE: new

L21: Entry 27 of 93

DOCUMENT-IDENTIFIER: US 20030082152 A1

TITLE: Adipose-derived stem cells and lattices

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

RULE-47 STATE COUNTRY CITY NAME US

CA Encino Hedrick, Marc H.

Katz, Adam J.	Charlottesville	VA	US
Llull, Ramon	Mallorca	PA	ES
Futrell, J. William	Pittsburgh	CA	US
Benhaim, Prosper	Encino	CA	US
Lorenz, Hermann Peter	Belmont	CA	US
Zhu, Min	Los Angeles		US

US-CL-CURRENT: 424/93.21; 435/366

#### ABSTRACT:

The present invention provides adipose-derived stem cells (ADSCs), adipose-derived stem cell-enriched fractions (ADSC-EF) and adipose-derivedlattices, alone and combined with the ADSCs of the invention. In one aspect, the present invention provides an ADSC substantially free of adipocytes and red blood cells and clonal populations of connective tissue stem cells. The ADSCs can be employed, alone or within biologically-compatible compositions, to generate differentiated tissues and structures, both in vivo and in vitro. Additionally, the ADSCs can be expanded and cultured to produce molecules such as hormones, and to provide conditioned culture media for supporting the growth and expansion of other cell populations. In another aspect, the present invention provides a adipose-derived lattice substantially devoid of cells, which includes extracellular matrix material from adipose tissue. The lattice can be used as a substrate to facilitate the growth and differentiation of cells, whether in vivo or in vitro, into anlagen or even mature tissues or structures.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims KMC Draw Desi
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		***************************************
☐ 28. Document ID: US 20030077823 A1	İ	
L21: Entry 28 of 93	File: PGPB	Apr 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030077823

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030077823 A1

TITLE: Nestin-expressing hair follicle stem cells

PUBLICATION-DATE: April 24, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Li, Lingna San Diego CA US
Yang, Meng San Diego CA US

US-CL-CURRENT: 435/366

#### ABSTRACT:

Hair follicle stem cells are isolated from mammals by isolating <u>nestin</u>-expressing cells. These hair follicle stem cells are a source of adult stem cells for autologous or heterologous stem cell therapy. The stem cells can be systemically implanted into the mammal or directly implanted into the organ. In addition, the stem cells may be further differentiated in vitro and then implanted systemically or directly into the mammal.

Citation Front Review Classification Date Reference Sequences Attachments Claims KWIC

# ☐ 29. Document ID: US 20030068819 A1

L21: Entry 29 of 93

File: PGPB

Apr 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030068819

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030068819 A1

TITLE: Method of in vitro differentiation of transplantatable neural precursor cells

from primate embryonic stem cells

PUBLICATION-DATE: April 10, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Zhang, Su-Chun	Madison	WI	US	
Thomson, James A.	Madison	WI	US	
Duncan, Ian David	Madison	WI	US .	

US-CL-CURRENT: 435/368

# ABSTRACT:

A method of differentiating embryonic stem cells into neural precursor cells is disclosed. In one embodiment the method comprises the steps of (a) obtaining an embryonic stem cell culture, (b) propagating the stem cells, (c) forming embryoid bodies from the stem cells, and (d) culturing the embryoid bodies in a medium containing an effective amount of fibroblast growth factor 2, wherein neural precursor cells will be generated and isolated.

Full   Title   Citation   Front   Review   Classification	Date Reference	Sequences Attachments	Claims K)	MC Draw Des
☐ 30. Document ID: US 2003004011	1 A1	•		27, 2003

PGPUB-DOCUMENT-NUMBER: 20030040111

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030040111 A1

TITLE: Differentiated cells suitable for <a href="human">human</a> therapy

PUBLICATION-DATE: February 27, 2003

INVENTOR-INFORMATION:

RULE-47 COUNTRY CITY STATE NAME US San Francisco CA Gold, Joseph D. US Portola Valley CA Lebkowski, Jane S.

US-CL-CURRENT: 435/368; 435/366, 435/370

## ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

Full Title Citation Front Review Classification Date	Reference   Sequences	Attachments Claims	KMMC   Drawn Desc
☐ 31. Document ID: US 20030032187 A1 L21: Entry 31 of 93	File: PGPB	Feb	13, 2003

PGPUB-DOCUMENT-NUMBER: 20030032187

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030032187 A1

TITLE: Selective antibody targeting of undifferentiated stem cells

PUBLICATION-DATE: February 13, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 McWhir, Jim Midlothian CA GB GOld, Joseph D. San Francisco CA US Schiff, J. Michael Menlo Park US

US-CL-CURRENT: 435/455; 435/366

#### ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in expression of a cell-surface antigen that can be used to deplete the undifferentiated cells. Model effector sequences encode glycosyl transferases that synthesize carbohydrate xenoantigen or alloantigen, which can be used for immunoseparation or as a target for complement-mediated lysis. The differentiated cell populations produced are suitable for use in tissue regeneration and non-therapeutic applications such as drug screening.

Full Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWAC	Draw Desi
	:										

# ☐ 32. Document ID: US 20030027331 A1

L21: Entry 32 of 93

File: PGPB

Feb 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030027331

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030027331 A1

TITLE: Isolated homozygous stem cells, differentiated cells derived therefrom, and

materials and methods for making and using same

PUBLICATION-DATE: February 6, 2003

TARRENGEOD	-TNFORMATION:
1 NIV #.NT CJR —	- LINE ORIMALLON -

NAME	CITY	STATE	COUNTRY	RULE-47
Yan, Wen Liang	Potomac	MD	US	
Huang, Steve Chien-Wen	Germantown	MD	US	
Nguyen, Minh-Thanh	Rockville	MD	US	
Lin, Hua	N. Potomac	MD	US	
Jingqi, Lei	Gaithersburg	MD	US	
Khanna, Ruchi	Germantown	MD	US	

US-CL-CURRENT: 435/366

## ABSTRACT:

The present invention discloses and describes pluripotent homozygous stem (HS) cells, and methods and materials for making same. The present invention also provides methods for differentiation of HS cells into progenitor (multipotent) cells or other desired cells, groups of cells or tissues. Further, the applications of the HS cells disclosed herein, include (but are not limited to) the diagnosis and treatment of various diseases (for example, genetic diseases, neurodegenerative diseases, endocrine-related disorders and cancer), traumatic injuries, cosmetic or therapeutic transplantation, gene therapy and cell replacement therapy.

Full   Title   Citation   Front   Review   Classification   Date	Reference   Sequences   /	Attachments Claims KMC Draw Desc
☐ 33. Document ID: US 20030013192 A1 L21: Entry 33 of 93	File: PGPB	Jan 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030013192

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030013192 A1

TITLE: Method for neural stem cell differentiation using valproate

PUBLICATION-DATE: January 16, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Laeng, Pascal	Washington	DC	US	
Mallon, Barbara	Gaithersburg	MD	US	
Pitts, Lee	Falls Church	VA	US	

US-CL-CURRENT: 435/368; 514/557

#### ABSTRACT:

The present invention relates to a method for differentiating a neural stem cell into a neuronal cell such as a neuroblast or neuron in vitro or in vivo. Particularly, the invention provides for a method for neural stem cell differentiation by contacting the neural stem cell with a valproate compound or analog thereof.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims	KMMC Draw Desc
☐ 34. Document ID: US 20030003574 A			
L21: Entry 34 of 93	File: PGPB	Ja	n 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030003574

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030003574 A1

TITLE: Multipotent stem cells from peripheral tissues and uses thereof

PUBLICATION-DATE: January 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Montreal		CA	
Akhavan, Mahnaz	Montreal		CA	
Fernandes, Karl J. L.	Montreal		. CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Montreal		CA	

US-CL-CURRENT: 435/368

# ABSTRACT:

This invention relates to multipotent stem cells, purified from the peripheral tissue of mammals, and capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Full   Title   Citation   Front   Review   Classific	sation   Date   Reference   Sequences   Atta	ichments   Claims   KWC   Draw. Desv
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☐ 35. Document ID: US 200201	68767 A1	
L21: Entry 35 of 93	File: PGPB	Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168767

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168767 A1

TITLE: Method of isolating <u>human</u> neuroepithelial precursor cells from <u>human</u> fetal tissue

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

CITY STATE COUNTRY RULE-47 NAME Pittsford NY Mayer-Proschel, Margot UT Salt Lake City US Rao, Mahendra S. Sandy UT US Tresco, Patrick A. UT US Salt Lake City Messina, Darin J.

US-CL-CURRENT: 435/368; 800/8

#### ABSTRACT:

A method for isolating <u>human</u> neuroepithelial precursor cells from <u>human</u> fetal tissue by culturing the <u>human</u> fetal cells in fibroblast growth factor and chick embryo extract and immunodepleting from the cultured <u>human</u> fetal cells any cells expressing A2B5, NG2 and eNCAM is provided. In addition, methods for transplanting these cells into an animal are provided. Animals models transplanted with these <u>human</u> neuroepithelial precursor cells and methods for monitoring survival, proliferation, differentiation and migration of the cells in the animal model via detection of <u>human</u> specific markers are also provided.

Full	Title Citation Front Review	Classification Date Reference	Sequences Attachments	Claims KWWC Draw. Desc
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				,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
	36. Document ID: US 2	0020168766 A1		
L21:	Entry 36 of 93	File	: PGPB	Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168766

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168766 A1

PUBLICATION-DATE: November 14, 2002

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Gold, Joseph D.	San Francisco	CA	US	
Carpenter, Melissa K.	Castro Valley	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Xu, Chunhui	Cupertino	CA	US	

US-CL-CURRENT: 435/366; 435/455

# ABSTRACT:

This disclosure provides a system for obtaining genetically altered primate pluripotent stem (pPS) cells. The pPS cells are maintained in an undifferentiated state by culturing on a feeder cell line that has been immortalized and altered with drug resistance genes. Alternatively, the role of the feeder cells is replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. The cells can be genetically altered with a viral vector or DNA/lipid complex, and then selected for successful transfection by drug-resistant phenotype in the transfected cells. The system allows for bulk proliferation of

genetically altered pPS cells as important products for use in  $\underline{\text{human}}$  therapy or drug screening.

Full Title Citation Front Review Classification	Date Reference Sequences Atta	ichments   Claims   KWIC   Draw Desi
☐ 37. Document ID: US 2002016876	63 A1	
L21: Entry 37 of 93	File: PGPB	Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168763

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168763 A1

TITLE: Isolated homozygous stem cells, differentiated cells derived therefrom, and materials and methods for making and using same

PUBLICATION-DATE: November 14, 2002

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yan, Wen Liang	Potomac	MD	US	
Huang, Steve Chien-Wen	Germantown	MD	ບຣ	
Nguyen, Minh-Thanh	Rockville	MD	US	
Lin, Hua (Helen)	Potomac	MD	US	
Lei, Jingqi	Gaithersburg	MD	US .	
Khanna, Ruchi	Germantown	MD	US	

US-CL-CURRENT: 435/325; 435/350, 435/354, 435/366

#### ABSTRACT:

The present invention discloses and describes pluripotent homozygous stem (HS) cells, and methods and materials for making same. The present invention also provides methods for differentiation of HS cells into progenitor (multipotent) cells or other desired cells, groups of cells or tissues. Further, the applications of the HS cells disclosed herein, include (but are not limited to) the diagnosis and treatment of various diseases (for example, genetic diseases, neurodegenerative diseases, endocrine-related disorders and cancer), traumatic injuries, cosmetic or therapeutic transplantation, gene therapy and cell replacement therapy.

Full Title Citation Front Review Classificatio	on Date Reference Sequences Attact	nments Claims KWC Draw Desc
☐ 38. Document ID: US 200201643		,
L21: Entry 38 of 93	File: PGPB	Nov 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020164308

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164308 A1

TITLE: Embryonic stem cells and neural progenitor cells derived therefrom

PUBLICATION-DATE: November 7, 2002

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U... 10/27/04

INVENTOR-INFORMATION:

NAME

STATE COUNTRY RULE-47

Reubinoff, Benjamin Eithan

Mevaseret Zign Prshrab Victoria IL

Pera, Martin Frederick

Ben-Hur, Tamir

Jerusalem

AU IL

US-CL-CURRENT: 424/93.7; 435/366, 435/368

#### ABSTRACT:

The present invention relates to undifferentiated <u>human</u> embryonic stem cells, methods of cultivation and propagation and production of differentiated cells. In particular it relates to the production of <u>human</u> ES cells capable of yielding somatic differentiated cells in vitro, as well as committed progenitor cells such as neural progenitor cells capable of giving rise to mature somatic cells including neural cells and/or glial cells and uses thereof.

This invention provides methods that generate in vitro and in vivo models of controlled differentiation of ES cells towards the neural lineage. The model, and cells that are generated along the pathway of neural differentiation may be used for: the study of the cellular and molecular biology of <a href="https://discovery.org/neural-development">https://discovery.org/neural-development</a>, and differentiation factors that play a role in neural differentiation and regeneration, drug discovery and the development of screening assays for teratogenic, toxic and neuroprotective effects.

Full	Title   Citation   Front   Review   Classification   Date					Draw Deso
	39. Document ID: US 20020151056 A1			·		
L21:	Entry 39 of 93	File:	PGPB		Oct 17,	2002

PGPUB-DOCUMENT-NUMBER: 20020151056

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020151056 A1

TITLE: Novel differentiation inducing process of embryonic stem cell to ectodermal

cell and its use

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Sasai, Yoshiki Kyoto JP Nishikawa, Shin-Ichi Kyoto JP

US-CL-CURRENT: 435/368

### ABSTRACT:

A method for inducing differentiation of an embryonic stem cell into an ectodermal cell and an ectoderm-derived cell, which comprises culturing the embryonic stem cell under non-aggregation conditions; a medium and a medium supernatant used in the method; an agent for inducing differentiation used in the method; a stroma cell or a stroma cell-derived factor having activity of inducing differentiation in the method; an antibody which specifically recognizes the stroma cell; an antigen which

recognizes the antibody; a cell induced by the method; a method for evaluating or screening a substance relating to the regulation in a differentiation step from an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell by carrying out the method; and a medicament comprising the stroma cell, the stroma cell-derived cell, the antibody, the antigen or the cell.

Full Title Citation Front Review	Classification Date Reference	Sequences Attachments	Claims KWC DraweDesc
☐ 40. Document ID: US 20	0020151053 A1		
L21: Entry 40 of 93	File:	PGPB	Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020151053

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020151053 A1

TITLE: Direct differentiation of <a href="https://doi.org/10.1001/journal.com/">https://doi.org/10.1001/journal.com/</a> pluripotent stem cells and characterization of

differentiated cells

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	
Funk, Walter D.	Hayward	CA	US	
Thies, R. Scott	Pleasanton	CA	US	

US-CL-CURRENT: 435/366

# ABSTRACT:

This invention provides a system for efficiently producing differentiated cells from pluripotent cells, such as <a href="https://www.nummons.com/mo

Full   Title   Citation   Front   Review   Classification	Date Reference Sequences Att	achments Claims KMC Draw Des
☐ 41. Document ID: US 2002014682	1 <b>A</b> 1	
L21: Entry 41 of 93	File: PGPB	oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020146821

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020146821 A1

TITLE: BONE MARROW CELLS AS A SOURCE OF NEURONS FOR BRAIN AND SPINAL CORD REPAIR

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U... 10/27/04

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
SANCHEZ-RAMOS, JUAN	TAMPA	FL	US	
SONG, SHIJIE	TAMPA	$\mathtt{FL}$	US	
JANSSEN, WILLIAM	TAMPA	FL	US	
SANBERG, PAUL	SPRING HILL	FL	US	
FREEMAN, THOMAS	TAMPA	FL	US	

US-CL-CURRENT:  $\underline{435}/\underline{368}$ ;  $\underline{435}/\underline{363}$ ,  $\underline{435}/\underline{366}$ ,  $\underline{435}/\underline{384}$ 

#### ABSTRACT:

Bone marrow stromal cells (BMSC) differentiate into neuron-like phenotypes in vitro and in vivo, engrafted into normal or denervated rat striatum. The BMSC did not remain localized to the site of the graft, but migrated throughout the brain and integrated into specific brain regions in various architectonic patterns. The most orderly integration of BMSC was in the laminar distribution of cerebellar Purkinje cells, where the BMSC-derived cells took on the Purkinje phenotype. The BMSC exhibited site-dependent differentiation and expressed several neuronal markers including neuron-specific nuclear protein, tyrosine hydroxylase and calbindin. BMSC can be used to target specific brain nuclei in strategies of neural repair and gene therapy.

Full	Title	Citation	Frent	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desc
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	42.	Docume	nt ID	: US 2	002014246	0 A1						
L21:	Entr	y 42 of	93				File	PGPB		0c	t 3,	2002

PGPUB-DOCUMENT-NUMBER: 20020142460

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020142460 A1

TITLE: Generation, characterization, and isolation of neuroepithelial stem cells and

lineage restricted intermediate precursor

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Rao, Mahendra S. Salt Lake City UT US
Mayer-Proschel, Margot Sandy UT US

US-CL-CURRENT: 435/368

# ABSTRACT:

Multipotent neuroepithelial stem cells and lineage-restricted oligodendrocyte-astrocyte precursor cells are described. The neuroepithelial stem cells are capable of self-renewal and of differentiation into neurons, astrocytes, and oligodendrocytes. The oligodendrocyte-astrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into oligodendrocytes and astrocytes, but not neurons. Methods of generating, isolating,

and culturing such neuroepithelial stem cells and oligodendrocyte-astrocyte precursor cells are also disclosed.

Full Title Citation Front Review Classification Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Des
·	***************************************	***************************************				
☐ 43. Document ID: US 20020137204 A1						
1.21: Entry 43 of 93	File:	PGPB		Sep	26,	2002

PGPUB-DOCUMENT-NUMBER: 20020137204

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020137204 A1

TITLE: Techniques for growth and differentiation of human pluripotent stem cells

PUBLICATION-DATE: September 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	•
Funk, Walter D.	Hayward	CA	US	
Gold, Joseph D.	San Francisco	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Xu, Chunhui	Cupertino	CA	US	

US-CL-CURRENT: 435/366

# ABSTRACT:

This disclosure provides an improved system for culturing <u>human</u> pluripotent stem (pPS) cells in the absence of feeder cells. The role of the feeder cells can be replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. Permanent cell lines are provided that can produce conditioned medium on a commercial scale. Methods have also been discovered to genetically alter pPS cells by introducing the cells with a viral vector or DNA/lipid complex. The system described in this disclosure allows for bulk proliferation of pPS cells for use in studying the biology of pPS cell differentiation, and the production of important products for use in <u>human</u> therapy.

Full Title Citation Front Review Classificat	tion Date Reference Sequences Attact	nments Claims KWC Draw Desc
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☐ 44. Document ID: US 20020123	3143 A1	
L21: Entry 44 of 93	File: PGPB	Sep 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020123143

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020123143 A1

TITLE: Multipotent stem cells from peripheral tissues and uses thereof

PUBLICATION-DATE: September 5, 2002

INVENTOR-INFORMATION:

STATE COUNTRY RULE-47 CITY NAME CA Montreal Toma, Jean CA Montreal Akhavan, Mahnaz Fernandes, Karl J. L. Montreal CA Orford CA Fortier, Mathieu CA Montreal Miller, Freda

US-CL-CURRENT: 435/368

#### ABSTRACT:

This invention relates to multipotent stem cells, purified from the peripheral tissue of mammals, and capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Full	Title Citation Front Review Classification Date	Reference	Sequences	Attachments	Claims	KMC	Draw, Desi
	45. Document ID: US 20020098582 A1						
L21:	Entry 45 of 93	File:	PGPB		Jul	25,	2002

PGPUB-DOCUMENT-NUMBER: 20020098582

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020098582 A1

TITLE: Differentiated stem cells suitable for human therapy

PUBLICATION-DATE: July 25, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Gold, Joseph D. San Francisco CA US

Lebkowski, Jane S. Portola Valley CA US

US-CL-CURRENT: 435/366; 424/93.21, 435/194

# ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

☐ 46. Document ID: US 20020090723 A1

L21: Entry 46 of 93

File: PGPB

Jul 11, 2002

PGPUB-DOCUMENT-NUMBER: 20020090723

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020090723 A1

TITLE: Techniques for growth and differentiation of human pluripotent stem cells

PUBLICATION-DATE: July 11, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE COUNTRY

RULE-47

Carpenter, Melissa K.

Castro Valley

CA

Inokuma, Margaret S.

San Jose

CA

US

US

Xu, Chunhui

Cupertino

CA

US

US-CL-CURRENT: 435/366; 435/368

#### ABSTRACT:

This disclosure provides an improved system for culturing <a href="https://www.nummons.com/human">human</a> pluripotent stem (pPS) cells in the absence of feeder cells. The role of the feeder cells can be replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. Permanent cell lines are provided that can produce conditioned medium on a commercial scale. Methods have also been discovered to genetically alter pPS cells by introducing the cells with a viral vector or DNA/lipid complex. The system described in this disclosure allows for bulk proliferation of pPS cells for use in studying the biology of pPS cell differentiation, and the production of important products for use in <a href="https://www.nummons.com/human">human</a> therapy.

Full	Title C	itation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Draw, Desk

☐ 47. Document ID: US 20020086005 A1

L21: Entry 47 of 93

File: PGPB

Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020086005

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020086005 A1

TITLE: Tolerizing allografts of pluripotent stem cells

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Chiu, Choy-Pik

Cupertino

CA

US

Kay, Robert M.

San Francisco

CA

US

US-CL-CURRENT: 424/93.21; 424/93.7, 435/366

## ABSTRACT:

This disclosure provides a system for overcoming HLA mismatch between an allograft derived from stem cells, and a patient being treated for tissue regeneration. A state of specific immune tolerance is induced in the patient, by administering a population of tolerizing cells derived from the stem cells. This allows the patient to accept an allograft of differentiated cells derived from the same source. This invention is important because it allows a single line of stem cells to act as a universal donor source for tissue regeneration in any patient, regardless of tissue type.

Full	Title	·	eview   Classification					
						 	*************	anmeenmanna.
	48.	Document ID:	US 20020081724	Al				
L21:	Entr	y 48 of 93		File:	PGPB	Jun	27,	2002

PGPUB-DOCUMENT-NUMBER: 20020081724

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020081724 A1

TITLE: Techniques for growth and differentiation of human pluripotent stem cells

PUBLICATION-DATE: June 27, 2002

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	
Funk, Walter D.	Hayward	CA	US	
Gold, Joseph D.	San Francisco	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Xu, Chunhui	Cupertino	CA	US	ı

US-CL-CURRENT: 435/366; 435/354, 435/384

# ABSTRACT:

This disclosure provides an improved system for culturing <u>human</u> pluripotent stem (pPS) cells in the absence of feeder cells. The role of the feeder cells can be replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. Permanent cell lines are provided that can produce conditioned medium on a commercial scale. Methods have also been discovered to genetically alter pPS cells by introducing the cells with a viral vector or DNA/lipid complex. The system described in this disclosure allows for bulk proliferation of pPS cells for use in studying the biology of pPS cell differentiation, and the production of important products for use in <u>human</u> therapy.

Full Title Citation Front Review Classification Dar	te Reference Sequences	Attachments Claims KWMC Draw Des	•
☐ 49. Document ID: US 20020068045 A	l File: PGPB	Jun 6, 2002	

PGPUB-DOCUMENT-NUMBER: 20020068045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020068045 A1

TITLE: Embryonic stem cells and neural progenitor cells derived therefrom

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Reubinoff, Benjamin Eithan Mevaseret-Zion IL

Pera, Martin Frederick Prahran AU
Ben-Hur, Tamir Ramat Sharet IL

US-CL-CURRENT: 424/93.7; 435/368

## ABSTRACT:

The present invention provides undifferentiated <u>human</u> embryonic stem cells, methods of cultivation and propagation and production of differentiated cells. In particular it relates to the production of <u>human</u> ES cells capable of yielding somatic differentiated cells in vitro, and committed progenitor cells such as neural progenitor cells capable of giving rise to mature somatic cells including neural cells and/or glial cells and uses thereof. The invention also provides methods that generate in vitro and in vivo models of controlled differentiation of ES cells towards the neural lineage. The model, and the cells that are generated along the pathway of neural differentiation may be used for the study of the cellular and molecular biology of <u>human</u> neural development, for the discovery of genes, growth factors, and differentiation factors that play a role in neural differentiation and regeneration, for drug discovery and for the development of screening assays for teratogenic, toxic and neuroprotective effects.

Full	Title	Citation	Front	Review	Classification	Date Referenc	se Sequences	Attachments	Claims	KWIC	Draw, Desi
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☐ 50. Document ID: US 20020045251 A1

L21: Entry 50 of 93 File: PGPB Apr 18, 2002

PGPUB-DOCUMENT-NUMBER: 20020045251

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020045251 A1

TITLE: COMMON NEURAL PROGENITOR FOR THE CNS AND PNS

PUBLICATION-DATE: April 18, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

RAO, MAHENDRA S. SALT LAKE CITY UT US MUJTABA, TAHMINA SANDY UT US

US-CL-CURRENT: 435/325; 435/368, 435/373, 435/377, 435/383, 435/384, 435/387, 435/391, 435/395, 435/402

ABSTRACT:

A method of generating neural crest stem cells involves inducing neuroepithelial stem cells to differentiate in vitro into neural crest stem cells. Differentiation can be induced by replating the cells on laminin, withdrawing mitogens, or adding dorsalizing agents to the growth medium. Derivatives of the peripheral nervous system can be generated by inducing the neural crest stem cells to differentiate in vitro.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw. Desc

☐ 51. Document ID: US 20020039724 A1

L21: Entry 51 of 93

File: PGPB

Apr 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020039724

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020039724 A1

TITLE: Neural progenitor cell populations

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE COUNTRY

RULE-47

Mar 14, 2002

Carpenter, Melissa K.

Castro Valley

CA

US

US-CL-CURRENT: 435/4; 435/368

### ABSTRACT:

This invention provides populations of neural progenitor cells, differentiated neurons, glial cells, and astrocytes. The populations are obtained by culturing stem cell populations (such as embryonic stem cells) in a cocktail of growth conditions that initiates differentiation, and establishes the neural progenitor population. The progenitors can be further differentiated in culture into a variety of different neural phenotypes, including dopaminergic neurons. The differentiated cell populations or the neural progenitors can be generated in large quantities for use in drug screening and the treatment of neurological disorders.

File: PGPB

PGPUB-DOCUMENT-NUMBER: 20020031497

PGPUB-FILING-TYPE: new

L21: Entry 52 of 93

DOCUMENT-IDENTIFIER: US 20020031497 A1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due to neurodegenerative diseases

PUBLICATION-DATE: March 14, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Fraser, Thomas Newton MA US
Dinsmore, Jonathan Brookline MA US

US-CL-CURRENT: 424/93.7; 435/325

### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims	KMC Draw Desi
☐ 53. Document ID: US 20020028510 A1			
L21: Entry 53 of 93	File: PGPB	Ma	ar 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020028510

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020028510 A1

TITLE: Human cord blood as a source of neural tissue for repair of the brain and

spinal cord

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Sanberg, Paul	Spring Hill	FL	US	
Sanchez-Remos, Juan	Tampa	FL	US	
Willing, Alison	Tampa	FL	US	
Richard, Daniel D.	Sedona	AZ	บร	

US-CL-CURRENT: 435/368

# ABSTRACT:

The present invention relates to the use of umbilical cord blood cells from a donor or patient to provide neural cells which may be used in transplantation. The isolated cells according to the present invention may be used to effect autologous and allogeneic transplantation and repair of neural tissue, in particular, tissue of the

brain and spinal cord and to treat neurodegenerative diseases of the brain and spinal cord.

			4
Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims KMC Draw Des	
☐ 54. Document ID: US 20020019046 A1			
	File: PGPB	Feb 14, 2002	
1.21: Entry 54 of 93	ETTC. EGED	100 11, 2002	

PGPUB-DOCUMENT-NUMBER: 20020019046

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020019046 A1

differentiated cells

PUBLICATION-DATE: February 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	
Funk, Walter D.	Hayward	CA	US	
Thies, R. Scott	Pleasanton	CA	US	

US-CL-CURRENT: 435/368; 435/4, 435/91.1

## ABSTRACT:

This invention provides a system for efficiently producing differentiated cells from pluripotent cells, such as <u>human</u> embryonic stem cells. Rather than permitting the cells to form embryoid bodies according to established techniques, differentiation is effected directly in monolayer culture on a suitable solid surface. The cells are either plated directly onto a differentiation-promoting surface, or grown initially on the solid surface in the absence of feeder cells and then exchanged into a medium that assists in the differentiation process. The solid surface and the culture medium can be chosen to direct differentiation down a particular pathway, generating a cell population that is remarkably uniform. The methodology is well adapted to bulk production of committed precursor and terminally differentiated cells for use in drug screening or regenerative medicine.

Full   Title   Citation   Front   Review   Classific	ation Date Reference Sequences Attact	nments Claims KWIC Draw Des
☐ 55. Document ID: US 200200	16002 A1	
L21: Entry 55 of 93	File: PGPB	Feb 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020016002

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020016002 A1

TITLE: Multipotent neural stem cells from peripheral tissues and uses thereof

PUBLICATION-DATE: February 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Montreal		CA	
Akhavan, Mahnaz	Montreal		CA	
Fernandes, Karl J. L.	Montreal		CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Montreal		CA	

US-CL-CURRENT: 435/368; 435/366

#### ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Full   Title   Citation   Front   Review   Classification   Date	Reference Sequences	Attachments Clair	ms KWIC Draw, Desi
☐ 56. Document ID: US 20020009743 A1		-	
L21: Entry 56 of 93	File: PGPB		Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020009743

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020009743 A1

TITLE: Neural progenitor cell populations

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Carpenter, Melissa K. Castro Valley CA US

US-CL-CURRENT: 435/6; 424/93.21, 435/368

## ABSTRACT:

This invention provides populations of neural progenitor cells, differentiated neurons, glial cells, and astrocytes. The populations are obtained by culturing stem cell populations (such as embryonic stem cells) in a cocktail of growth conditions that initiates differentiation, and establishes the neural progenitor population. The progenitors can be further differentiated in culture into a variety of different neural phenotypes, including dopaminergic neurons. The differentiated cell populations or the neural progenitors can be generated in large quantities for use in drug screening and the treatment of neurological disorders.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw Desi	
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L21: Entry 57 of 93 File: PGPB Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020009461

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020009461 A1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due

to neurodegenerative diseases

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Isacson, Ole Cambridge MA US
Dinsmore, Jonathan Brookline MA US

US-CL-CURRENT: 424/193.1; 424/93.7, 435/325

#### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

Full	Title	Citation Front F	eview	Claszification	Date	Reference	Sequences	Attachments	Claims	KAMIC	Drawu Desc
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	58.	Document ID:	US 20	020004039	9 <b>A</b> 1						

File: PGPB

PGPUB-DOCUMENT-NUMBER: 20020004039

PGPUB-FILING-TYPE: new

L21: Entry 58 of 93

DOCUMENT-IDENTIFIER: US 20020004039 A1

TITLE: Methods for treating neurological deficits

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Reid, James Steven Berkeley CA US
Fallon, James H. Irvine CA US

Jan 10, 2002

US-CL-CURRENT: 424/93.7; 435/368

## ABSTRACT:

The present invention features methods and compositions for treating a patient who has a neurological deficit. The method can be carried out, for example, by contacting (in vivo or in culture) a neural progenitor cell of the patient's central nervous system (CNS) with a polypeptide that binds the epidermal growth factor (EGF) receptor and directing progeny of the proliferating progenitor cells to migrate en masse to a region of the CNS in which they will reside and function in a manner sufficient to reduce the neurological deficit. The method may include a further step in which the progeny of the neural precursor cells are contacted with a compound that stimulates differentiation.

Full	Title Citation Front Review Classification Date	Reference Sequences		
	59. Document ID: US 20010055808 A1	and the second		
1.21:	Entry 59 of 93	File: PGPB	Dec	27. 2001

PGPUB-DOCUMENT-NUMBER: 20010055808

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010055808 A1

TITLE: Use of collagenase in the preparation of neural stem cell cultures

PUBLICATION-DATE: December 27, 2001

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Uchida, Nobuko Palo Alto CA US

US-CL-CURRENT: 435/368

# ABSTRACT:

The invention provides a method for using collagenase to dissociate neural stem cells in neural stem cell cultures. The collagenase treatment results in an increased cell viability and an increased number of proliferated neural stem cells over time.

Full Title Citation Front Review Classification Date	Reference	Sequences	Attachments	Claims	KWMC	Drawi Desc
	***************************************					***************************************
☐ 60. Document ID: US 20010033834 A1						
L21: Entry 60 of 93	File:	PGPB		Oct	25,	2001

PGPUB-DOCUMENT-NUMBER: 20010033834

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010033834 A1

TITLE: Pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof

PUBLICATION-DATE: October 25, 2001

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Wilkison, William O. Bahama NC US
Gimble, Jeffrey Chapel Hill NC US

US-CL-CURRENT: 424/93.7; 424/93.21, 435/325, 435/366, 435/368, 435/372

#### ABSTRACT:

The invention is in the area of pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof. In particular, the invention includes isolated adipose tissue derived stromal cells that have been induced to express at least one phenotypic characteristic of a neuronal, astroglial, hematopoietic progenitor, or hepatic cell. The invention also includes an isolated adipocyte tissue-derived stromal cell that has been dedifferentiated such that there is an absence of adipocyte phenotypic markers.

Full Title Citation Front	Review Classification Date	e Reference Sequences	Attachments   Claims   KMC   Draw Desi

☐ 61. Document ID: US 20010029045 A1

L21: Entry 61 of 93 File: PGPB Oct 11, 2001

PGPUB-DOCUMENT-NUMBER: 20010029045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010029045 A1

TITLE: Lineage restricted glial precursors from the central nervous system

PUBLICATION-DATE: October 11, 2001

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Rao, Mahendra S. Salt Lake City UT US
Noble, Mark Brighton NY US
Mayer-Proschel, Margot Pittsford NY US

US-CL-CURRENT: 435/325; 424/93.7

#### ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

Full Title Citation	Front Review Classific	ation Date Reference	Sequences Attachmen	s Claims KWC	Draw, Desi
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# ☐ 62. Document ID: US 6787355 B1

L21: Entry 62 of 93

File: USPT

Sep 7, 2004

Sep 7, 2004

US-PAT-NO: 6787355

DOCUMENT-IDENTIFIER: US 6787355 B1

TITLE: Multipotent neural stem cells from peripheral tissues and uses thereof

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Miller; Freda D. Montreal CA
Gloster; Andrew Saskatoon CA

Toma; Jean Montreal CA

US-CL-CURRENT: 435/377; 435/325, 435/375, 435/378, 435/383

## ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

8 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full	Title	Citation	Front	Review	Classification	n Date	Reference		Claims	KWIC	Draw, Desi
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	63.	Docum	ent ID	: US 6	787353 B	1		•			

File: USPT

US-PAT-NO: 6787353

L21: Entry 63 of 93

DOCUMENT-IDENTIFIER: US 6787353 B1

TITLE: Lineage-restricted neuronal precursors and methods of isolation

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Rao; Mahendra S. Salt Lake City UT
Mayer-Proschel; Margot Sandy UT

Kalyani; Anjali J. Salt Lake City UT

US-CL-CURRENT: 435/368; 435/377

### ABSTRACT:

A self-renewing restricted stem cell population has been identified in developing (embryonic day 13.5) spinal cords that can differentiate into multiple neuronal

phenotypes, but cannot differentiate into glial phenotypes. This neuronal-restricted precursor (NRP) expresses highly polysialated or embryonic neural cell adhesion molecule (E-NCAM) and is morphologically distinct from neuroepithelial stem cells (NEP cells) and spinal glial progenitors derived from embryonic day 10.5 spinal cord. NRP cells self renew over multiple passages in the presence of fibroblast growth factor (FGF) and neurotrophin 3 (NT-3) and express a characteristic subset of neuronal epitopes. When cultured in the presence of RA and the absence of FGF, NRP cells differentiate into GABAergic, glutaminergic, and cholinergic immunoreactive neurons. NRP cells can also be generated from multipotent NEP cells cultured from embryonic day 10.5 neural tubes. Clonal analysis shows that E-NCAM immunoreactive NRP cells arise from an NEP progenitor cell that generates other restricted CNS precursors. The NEP-derived E-NCAM immunoreactive cells undergo self renewal in defined medium and differentiate into multiple neuronal phenotypes in mass and clonal culture. Thus, a direct lineal relationship exists between multipotential NEP cells and more restricted neuronal precursor cells present in vivo at embryonic day 13.5 in the spinal cord. Methods for treating neurological diseases are also disclosed.

7 Claims, 14 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 10

Full		tion   Front   Review   Classification		•	Claims KMC	Draw. Desc
		cument ID: US 6734015 B1				
L21:	Entry 6	1 of 93	File:	USPT	May 11,	2004

US-PAT-NO: 6734015

DOCUMENT-IDENTIFIER: US 6734015 B1

TITLE: Isolation of lineage-restricted neuronal precursors

DATE-ISSUED: May 11, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Rao; Mahendra S. Salt Lake City UT Mayer-Proschel; Margot Sandy UT

US-CL-CURRENT: 435/368; 435/325

# ABSTRACT:

A self-renewing restricted stem cell population has been identified in developing (embryonic day 13.5) spinal cords that can differentiate into multiple neuronal phenotypes, but cannot differentiate into glial phenotypes. This neuronal-restricted precursor (NRP) expresses highly polysialated or embryonic neural cell adhesion molecule (E-NCAM) and is morphologically distinct from neuroepithelial stem cells (NEP cells) and spinal glial progenitors derived from embryonic day 10.5 spinal cord. NRP cells self renew over multiple passages in the presence of fibroblast growth factor (FGF) and neurotrophin 3 (NT-3) and express a characteristic subset of neuronal epitopes. When cultured in the presence of RA and the absence of FGF, NRP cells differentiate into GABAergic, glutaminergic, and cholinergic immunoreactive neurons. NRP cells can also be generated from multipotent NEP cells cultured from embryonic day 10.5 neural tubes. Clonal analysis shows that E-NCAM immunoreactive NRP cells arise from an NEP progenitor cell that generates other restricted CNS precursors. The NEP-derived E-NCAM immunoreactive cells undergo self renewal in defined medium and differentiate into multiple neuronal phenotypes in mass and clonal

culture. Thus, a direct lineal relationship exists between multipotential NEP cells and more restricted neuronal precursor cells present in vivo at embryonic day 13.5 in the spinal cord.

1 Claims, 1 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 1

Full Title Citation Front Review Classification D		Claims KWMC Drawx Deso
☐ 65. Document ID: US 6667176 B1		
L21: Entry 65 of 93	File: USPT	Dec 23, 2003

US-PAT-NO: 6667176

DOCUMENT-IDENTIFIER: US 6667176 B1

TITLE: cDNA libraries reflecting gene expression during growth and differentiation of

human pluripotent stem cells

DATE-ISSUED: December 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Funk; Walter D.	Hayward	CA		
Carpenter; Melissa K.	Foster City	CA		
Gold; Joseph D.	San Francisco	CA		
Inokuma; Margaret S.	San Jose	CA		
Xu; Chunhui	Cupertino	CA		

US-CL-CURRENT:  $\underline{435}/\underline{363}$ ;  $\underline{435}/\underline{320.1}$ ,  $\underline{435}/\underline{366}$ ,  $\underline{435}/\underline{377}$ ,  $\underline{536}/\underline{23.1}$ 

#### ABSTRACT:

This disclosure provides a system for obtaining expression libraries from primate pluripotent stem (pPS) cells. pPS cells can be maintained in vitro without requiring a layer of feeder cells to inhibit differentiation. The role of the feeder cells is replaced by several other culture conditions provided in a suitable combination. Conditions that promote pPS cell growth without differentiation include supporting the culture on an extracellular matrix, and culturing the cells in a medium conditioned by another cell type. The cDNA libraries from such cultures are devoid of transcripts of feeder cell origin, relatively uncontaminated by transcripts from differentiated cells, and can have a high proportion of full-length transcripts. Subtraction libraries can also be produced that are enriched for transcripts modulated during differentiation.

27 Claims, 11 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 10

Full Title	Citation Front	Review	Classification	Date	Reference	Cla	ims KWC	Draw, Des
	•			•				
П 66	Document ID:	LIS 66	660837 B1	***************************************				

L21: Entry 66 of 93 File: USPT Dec 9, 2003

US-PAT-NO: 6660837

DOCUMENT-IDENTIFIER: US 6660837 B1

TITLE: Modified protein derived from protein kinase N

DATE-ISSUED: December 9, 2003

INVENTOR-INFORMATION:

NAME

Kaibuchi; Kozo

Ikoma

Toyonaka

Toyonaka

Iwamatsu; Akihiro

CITY

STATE

ZIP CODE

JP

JP

US-CL-CURRENT:  $\underline{530}/\underline{350}$ ;  $\underline{435}/\underline{194}$ ,  $\underline{435}/\underline{252.3}$ ,  $\underline{435}/\underline{252.33}$ ,  $\underline{435}/\underline{320.1}$ ,  $\underline{435}/\underline{325}$ ,  $\underline{530}/\underline{300}$ ,  $\underline{536}/\underline{23.1}$ ,  $\underline{536}/\underline{23.2}$ ,  $\underline{536}/\underline{23.5}$ 

#### ABSTRACT:

A object of the present invention is to provide a peptide inhibiting tumorigenesis or metastasis. The present invention is a peptide or derivatives thereof comprising a modified amino acid sequence of Protein Kinase N having the activated Rho protein binding activity and not having protein kinase activity, and a peptide or derivatives thereof comprising a modified amino acid sequence of Protein Kinase N inhibiting the protein kinase activity of Protein Kinase N or the enhancement of the activity and not having protein kinase activity.

5 Claims, 49 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 41

Full Title Citation Front Review Classificatio	n Date Reference	Claims KMMC Draw. Desc
☐ 67. Document ID: US 6638763 B	31	
L21: Entry 67 of 93	File: USPT	Oct 28, 2003

US-PAT-NO: 6638763

DOCUMENT-IDENTIFIER: US 6638763 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Isolated mammalian neural stem cells, methods of making such cells

DATE-ISSUED: October 28, 2003

INVENTOR-INFORMATION:

CITY	STATE	ZIP CODE	COUNTRY
Memphis	TN		
Memphis	TN		
Memphis	TN		
Johnson City	TN		
	Memphis Memphis Memphis	Memphis TN Memphis TN Memphis TN	Memphis TN Memphis TN Memphis TN

US-CL-CURRENT: 435/368; 435/325, 435/377, 435/384

#### ABSTRACT:

Using a novel culture approach, previously unknown populations of neural progenitor cells have been found within an adult mammalian brain. By limiting cell-cell contact, dissociated adult brain yields at least two types of cell aggregates. These aggregates or clones of stem/precursor cells can be generated from adult brain tissue with significantly long postmortem intervals. Both neurons and glia arise from stem/precursor cells of these cultures, and the cells can survive transplantation to the adult mammalian brain.

1 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 7

US-PAT-NO: 6576464

DOCUMENT-IDENTIFIER: US 6576464 B2

TITLE: Methods for providing differentiated stem cells

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

ZIP CODE

Gold; Joseph D.

San Francisco

CA

COUNTRI

Lebkowski; Jane S.

Portola Valley

CA

US-CL-CURRENT: 435/325; 536/23.1, 536/23.4, 536/24.1, 536/25.5

## ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

30 Claims, 10 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 10

Full Title Citation Front Review Classification Date Reference Claims KMC Draw Des	
Title Citation Tions	25)
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# ☐ 69. Document ID: US 6528245 B2

L21: Entry 69 of 93

File: USPT

Mar 4, 2003

US-PAT-NO: 6528245

DOCUMENT-IDENTIFIER: US 6528245 B2

TITLE: Bone marrow cells as a source of neurons for brain and spinal cord repair

DATE-ISSUED: March 4, 2003

INVENTOR-INFORMATION:

ZIP CODE COUNTRY STATE CITY NAME Tampa Sanchez-Ramos; Juan Song; Shijie Tampa FLTampa FLJanssen; William Spring Hill Sanberg; Paul FT. Tampa Freeman; Thomas

US-CL-CURRENT: 435/1.1; 435/325, 435/368

#### ABSTRACT:

Bone marrow stromal cells (BMSC) differentiate into neuron-like phenotypes in vitro and in vivo, engrafted into normal or denervated rat striatum. The BMSC did not remain localized to the site of the graft, but migrated throughout the brain and integrated into specific brain regions in various architectonic patterns. The most orderly integration of BMSC was in the laminar distribution of cerebellar Purkinje cells, where the BMSC-derived cells took on the Purkinje phenotype. The BMSC exhibited site-dependent differentiation and expressed several neuronal markers including neuron-specific nuclear protein, tyrosine hydroxylase and calbindin. BMSC can be used to target specific brain nuclei in strategies of neural repair and gene therapy.

5 Claims, 32 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 9

Draw, Des	KWIC	aims Ki	Cla				eference	te F	Da	ation	Classifica	Review	ſ	Front	itation	į	Γitle		Full
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2002	17,	Dec 1			Т	USP'	File:							93	70 of	У	ntr	: E	21:
	17,	Dec 1			Т	USP'	File:							93	70 of 95364				

DOCUMENT-IDENTIFIER: US 6495364 B2

TITLE: Mx-1 conditionally immortalized cells

DATE-ISSUED: December 17, 2002

INVENTOR-INFORMATION:

ZIP CODE COUNTRY CITY STATE NAME

Barrington RT Hammang; Joseph P. Messing; Albee Madison WT

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U...

US-CL-CURRENT: 435/320.1; 424/93.2, 435/325, 435/455, 514/44

#### ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inhibiting compound or a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

2 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full T	tle Citation	Front	Review	Classification	Date	Reference		Claims	KWIC	Draw, Des
□ 7	l. Docum	nent ID	: US 6	392118 B1						
L21: Er	try 71 o	£ 93				File:	USPT	May	21,	2002

US-PAT-NO: 6392118

DOCUMENT-IDENTIFIER: US 6392118 B1

TITLE: Mx-1 conditionally immortalized cells

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Hammang; Joseph P. Barrington RI
Messing; Albee Madison WI

US-CL-CURRENT: 800/14; 424/93.21, 435/320.1, 435/325, 435/455, 800/25

## ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

12 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

# ☐ 72. Document ID: US 6361996 B1

L21: Entry 72 of 93

File: USPT

Mar 26, 2002

US-PAT-NO: 6361996

DOCUMENT-IDENTIFIER: US 6361996 B1

TITLE: Neuroepithelial stem cells and glial-restricted intermediate precursors

DATE-ISSUED: March 26, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE ZIP CODE COUNTRY

Rao; Mahendra S.

Salt Lake City

UT

Mayer-Proschel; Margot

Sandy

UТ

US-CL-CURRENT: 435/353; 435/325

#### ABSTRACT:

Multipotent neuroepithelial stem cells and lineage-restricted oligodendrocyteastrocyte precursor cells are described. The neuroepithelial stem cells are capable of self-renewal and of differentiation into neurons, astrocytes, and oligodendrocytes. The oligodendrocyte-astrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into oligodendrocytes and astrocytes, but not neurons. Methods of generating, isolating, and culturing such neuroepithelial stem cells and oligodendrocyte-astrocyte precursor cells are also disclosed.

19 Claims, 2 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	KMMC D	ram, Desc
							;				

# ☐ 73. Document ID: US 6294383 B1

L21: Entry 73 of 93

File: USPT

Sep 25, 2001

US-PAT-NO: 6294383

DOCUMENT-IDENTIFIER: US 6294383 B1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due

to neurodegenerative diseases

DATE-ISSUED: September 25, 2001

INVENTOR-INFORMATION:

NAME CITY STATE

ZIP CODE

COUNTRY

Isacson; Ole

Cambridge

MA

Dinsmore; Jonathan

Brookline

MΆ

US-CL-CURRENT: 435/379; 435/325

#### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

8 Claims, 49 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 21

Full Titl	e Citation Front Review Classificat	tion Date Reference	Claims KWIC Draw, Desc
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	Document ID: US 6277372		
L21: Ent	cry 74 of 93	File: USPT	Aug 21, 2001

US-PAT-NO: 6277372

DOCUMENT-IDENTIFIER: US 6277372 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Porcine neural cells and their use in treatment of neurological deficits due to neurodegenerative diseases

DATE-ISSUED: August 21, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Fraser; Thomas Newton MA
Dinsmore; Jonathan Brookline MA

US-CL-CURRENT:  $\underline{424}/\underline{93.7}$ ;  $\underline{424}/\underline{93.1}$ ,  $\underline{435}/\underline{325}$ 

#### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a <a href="https://www.neural.cells.com/memodified">https://www.neural.cells.com/memodified</a> such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment

or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a <a href="https://www.neurophic.neuroph

10 Claims, 43 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 21

	· ·	
Full Title Citation Front Review Classi	ication Date Reference	Claims KMC Draw, Des
☐ 75. Document ID: US 625835	53 B1	
1.21 Entry 75 of 93	File: USPT	Jul 10, 2001

US-PAT-NO: 6258353

DOCUMENT-IDENTIFIER: US 6258353 B1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due

to neurodegenerative diseases

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Isacson; Ole Cambridge MA
Dinsmore; Jonathan Brookline MA

 $\text{US-CL-CURRENT:} \ \underline{424/93.1}; \ \underline{424/130.1}, \ \underline{424/143.1}, \ \underline{424/809}, \ \underline{424/93.7}, \ \underline{435/325}, \ \underline{435/368}$ 

## ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

26 Claims, 62 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 24

## ☐ 76. Document ID: US 6238922 B1

L21: Entry 76 of 93

File: USPT

May 29, 2001

US-PAT-NO: 6238922

DOCUMENT-IDENTIFIER: US 6238922 B1

TITLE: Use of collagenase in the preparation of neural stem cell cultures

DATE-ISSUED: May 29, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Uchida; Nobuko

Palo Alto

CA

US-CL-CURRENT: 435/380; 435/368, 435/378, 435/381

#### ABSTRACT:

The invention provides a method for using collagenase to dissociate neural stem cells in neural stem cell cultures when passaging aggregated neural stem cells. The collagenase treatment results in an increased cell viability and an increased number of proliferated neural stem cells over time.

34 Claims, 1 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 1

Full   Title   Citation   Front   Review   Classificati		
☐ 77. Document ID: US 6235527	•	
L21: Entry 77 of 93	File: USPT	May 22, 2001

US-PAT-NO: 6235527

DOCUMENT-IDENTIFIER: US 6235527 B1

TITLE: Lineage restricted glial precursors from the central nervous system

DATE-ISSUED: May 22, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE ZIP CODE

COUNTRY

Rao; Mahendra S.

Salt Lake City

UT

Noble; Mark

Sandy

UT

Mayer-Proschel; Margot

Sandy

UT

US-CL-CURRENT: 435/325; 435/368, 435/378, 435/395, 435/402

## ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

5 Claims, 0 Drawing figures Exemplary Claim Number: 1

Title Citation Front Review Classification Date Reference Claims KWIC Draw Description 78. Document ID: US 6214334 B1

L21: Entry 78 of 93 File: USPT Apr 10, 2001

US-PAT-NO: 6214334

DOCUMENT-IDENTIFIER: US 6214334 B1

\*\* See image for <u>Certificate</u> of <u>Correction</u> \*\*

TITLE: Compositions and methods for producing and using homogenous neuronal cell transplants to treat neurodegenerative disorders and brain and spinal cord injuries

COUNTRY

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE

Lee; Virginia M. -Y. Philadelphia PA

Trojanowski; John Q. Philadelphia PA

US-CL-CURRENT: 424/93.1; 424/93.7, 435/325, 435/347, 435/353

## ABSTRACT:

Methods of treating individuals suspected of suffering from diseases, conditions or disorders of the Central Nervous System which comprise implanting stable, homogeneous post-mitotic <a href="https://man.neurons.into">human</a> neurons into the individual's brain are disclosed. Methods of treating individuals suspected of suffering from injuries, diseases, conditions or disorders characterized by nerve damage which comprise implanting stable, homogeneous post-mitotic <a href="https://man.neurons.into">human</a> neurons at or near a site of said nerve damage are also disclosed.

6 Claims, 21 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

Full   Title   Citation   Front   Review   Classification   Da	ate Reference	Claims KMC Draw Desc
☐ 79. Document ID: US 6204053 B1		
L21: Entry 79 of 93	File: USPT	Mar 20, 2001

US-PAT-NO: 6204053

DOCUMENT-IDENTIFIER: US 6204053 B1

## \*\* See image for Certificate of Correction \*\*

TITLE: Porcine cortical cells and their use in treatment of neurological deficits due to neurodegenerative diseases

·

DATE-ISSUED: March 20, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE ZIP CODE

COUNTRY

Dinsmore; Jonathan

Brookline

MA

US-CL-CURRENT: 435/325; 424/93.7, 435/374

ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

16 Claims, 49 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 19

Full   Title   Citation   Front   Review   Classification   C	Date Reference	Claims KVMC Draw. Desc
☐ 80. Document ID: US 6140116 A		
L21: Entry 80 of 93	File: USPT	Oct 31, 2000

US-PAT-NO: 6140116

DOCUMENT-IDENTIFIER: US 6140116 A

\*\* See image for Certificate of Correction \*\*

TITLE: Isolated and modified porcine cerebral cortical cells

DATE-ISSUED: October 31, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Dinsmore; Jonathan Brookline MA

US-CL-CURRENT: 435/325; 424/93.7, 435/374

#### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

27 Claims, 40 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 21

Full Title Citation Front Review Classification Date Reference Claims KMC Draw. Des

81. Document ID: US 6040180 A

L21: Entry 81 of 93 File: USPT Mar 21, 2000

US-PAT-NO: 6040180

DOCUMENT-IDENTIFIER: US 6040180 A

TITLE: In vitro generation of differentiated neurons from cultures of mammalian

multipotential CNS stem cells

DATE-ISSUED: March 21, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE

Johe; Karl K. Potomac MD

US-CL-CURRENT: 435/377; 435/325, 435/353, 435/368

## ABSTRACT:

The present invention reveals in vitro cultures of region-specific, terminally differentiated, mature neurons derived from cultures of mammalian multipotential CNS stem cells and an in vitro procedure by which the differentiated neurons may be generated. The procedure involves the culturing of multipotential CNS stem cells from a specific region in a chemically defined serum-free culture medium containing a growth factor; replacing the medium with growth factor-free medium; harvesting the stem cells by trypsinization; plating the stem cells at a density of between 100,000 to 250,000 cells per square centimeter; and culturing the stem cells in a glutamic acid-free chemically defined serum-free culture medium.

COUNTRY

6 Claims, 80 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 23

Full Title Citation Front Review Classification Date Reference

Claims KWWC Draw Desi

☐ 82. Document ID: US 6033906 A

L21: Entry 82 of 93

File: USPT

Mar 7, 2000

US-PAT-NO: 6033906

DOCUMENT-IDENTIFIER: US 6033906 A

TITLE: Methods for differentiating neural stem cells to glial cells using neuregulins

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

CA

US-CL-CURRENT: 435/325; 435/353, 435/368

## ABSTRACT:

Method for producing a population of mammalian glial cells comprising contacting at least one mammalian neural stem cell with a culture medium containing a neuregulin and detecting the differentiation of stem cell to a population of glial cells.

17 Claims, 60 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 22

Full	little	Uttation	Front	Meniem :	UNISS	moznen ;	Uat	=	ı

□ 83. Document ID: US 6001654 A

L21: Entry 83 of 93

File: USPT

Reference

Dec 14, 1999

US-PAT-NO: 6001654

DOCUMENT-IDENTIFIER: US 6001654 A

\*\* See image for Certificate of Correction \*\*

TITLE: Methods for differentiating neural stem cells to neurons or smooth muscle cells using TGT-.beta. super family growth factors

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

Anderson; David J.

Altadena

ZIP CODE

COUNTRY

CA

Shah; Nirao M.

New York

NΥ

US-CL-CURRENT: 435/377; 435/325, 435/352, 435/353, 435/368, 435/375

## ABSTRACT:

Method for producing a population of mammalian neurons and/or smooth muscle cells comprising contacting at least one mammalian neural stem cell with a culture medium containing one or more growth factors from the TGF-.beta. super family and detecting the differentiation of stem cell to a population of neurons or smooth muscle cells.

22 Claims, 25 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 28

Full Title Citation Front Review Classification Date Reference Classification Date Reference Classification Date Reference Claims KMC Draws Design State Claims Claims Claims KMC Draws Design State Claims Claims KMC Draws Design State Claims Claims Claims KMC Draws Design State Claims Claims Claims KMC Draws Design State Claims Cla

US-PAT-NO: 5928947

DOCUMENT-IDENTIFIER: US 5928947 A

TITLE: Mammalian multipotent neural stem cells

DATE-ISSUED: July 27, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA

Stemple; Derek L. Newton MA

US-CL-CURRENT:  $\underline{435}/\underline{455}$ ;  $\underline{424}/\underline{93.7}$ ,  $\underline{435}/\underline{325}$ ,  $\underline{435}/\underline{440}$ ,  $\underline{435}/\underline{69.1}$ 

#### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

6 Claims, 20 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 22

Full Title Citation Front Review Classification Date Reference **1000 (1000)** Claims KMC Draw Desi

☐ 85. Document ID: US 5849553 A

L21: Entry 85 of 93 File: USPT Dec 15, 1998

US-PAT-NO: 5849553

DOCUMENT-IDENTIFIER: US 5849553 A

TITLE: Mammalian multipotent neural stem cells

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA

Stemple; Derek L. Newton MA

US-CL-CURRENT:  $\underline{435}/\underline{467}$ ;  $\underline{435}/\underline{320.1}$ ,  $\underline{435}/\underline{325}$ ,  $\underline{435}/\underline{353}$ ,  $\underline{435}/\underline{368}$ ,  $\underline{435}/\underline{455}$ ,  $\underline{435}/\underline{462}$ ,

435/69.1

#### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell, and immortalized cell lines which are capable of subsequent disimmortalization. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

25 Claims, 111 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 44

Full   Title   Citation   Front   Review   Classification   D	ate Reference	Claims   KMC   Draw, Des
☐ 86. Document ID: US 5840576 A		
L21: Entry 86 of 93	File: USPT	Nov 24, 1998

US-PAT-NO: 5840576

DOCUMENT-IDENTIFIER: US 5840576 A

TITLE: Methods and compositions of growth control for cells encapsulated within

bioartificial organs

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Schinstine; Malcolm Ben Salem PA

CA Toronto Shoichet; Molly S. Gentile; Frank T. Warwick RΙ Barrington RΙ Hammang; Joseph P. Horsham PA Holland; Laura M. Everett MA Cain; Brian M. MA Doherty; Edward J. Mansfield Smithfield RI Winn; Shelley R. CH Lutry Aebischer; Patrick

US-CL-CURRENT: 435/325; 435/375, 435/377, 435/400

#### ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

4 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full   Title   Citation   Front   Review   Classification   (	Date Reference	Claims KMC Draw Des
☐ 87. Document ID: US 5824489 A		
L21: Entry 87 of 93	File: USPT	Oct 20, 1998

US-PAT-NO: 5824489

DOCUMENT-IDENTIFIER: US 5824489 A

TITLE: In vitro method for obtaining an isolated population of mammalian neural crest stem cells

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Pasadena CA

US-CL-CURRENT: 435/7.21; 435/325, 435/375, 435/377, 435/378, 435/395, 435/402

## ABSTRACT:

The invention includes methods for the isolation and clonal propagation of mammalian neural stem cells. The methods employ a novel separation and culturing regimen and bioassays for establishing the generation of neural stem cell derivatives. These methods result in the production of non-transformed neural stem cells and their

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.22&ref=21&dbname=PGPB,USPT,U... 10/27/04

progeny. The invention demonstrates, at the clonal level, the self regeneration and asymmetrical division of mammalian neural stem cells for the first time in feeder cell-independent cultures. Lineage restriction is demonstrated within a developing clone and is shown to be sensitive to the local environment. Multipotent neural stem cells cultured on a mixed substrate of poly-D-lysine and fibronectin generate PNS neurons and glia, but on fibronectin alone the stem cells generate PNS glia but not neurons. The neurogenic potential of the stem cells, while not expressed, is maintained over time on fibronectin. The invention further includes transplantation assays which allow for the identification of mammalian neural stem cells from various tissues. It also includes methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals.

21 Claims, 48 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 16

Full Title Citation Front Review Classification Date Reference Claims RWC Draw Description Base Reference Reference Reference RWC Draw Description Base RWC Draw Description Base Reference RWC Draw Description Base RWC Draw Descrip

US-PAT-NO: 5792900

DOCUMENT-IDENTIFIER: US 5792900 A

\*\* See image for Certificate of Correction \*\*

TITLE: Compositions and methods for producing and using homogenous neuronal cell transplants

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE

Lee; Virginia M.-Y. Philadelphia PA Trojanowski; John Q. Philadelphia PA

US-CL-CURRENT: 800/12; 424/93.1, 424/93.2, 424/93.21, 424/93.7, 435/325, 435/368, 435/69.7, 435/70.1, 435/71.1, 800/9

COUNTRY

#### ABSTRACT:

11 Claims, 20 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full Title Citation Front	Review Classification Date Refere	nce Claims	KMMC Draw Desc
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L21: Entry 89 of 93 File: USPT May 19, 1998

US-PAT-NO: 5753506

DOCUMENT-IDENTIFIER: US 5753506 A

TITLE: Isolation propagation and directed differentiation of stem cells from

embryonic and adult central nervous system of mammals

DATE-ISSUED: May 19, 1998

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Johe; Karl K.

Potomac

MD

US-CL-CURRENT: 435/377; 435/325, 435/366, 435/368

## ABSTRACT:

The present invention reveals an in vitro procedure by which a homogeneous population of multipotential precursor cells from mammalian embryonic neuroepithelium (CNS stem cells) can be expanded up to 10.sup.9 fold in culture while maintaining their multipotential capacity to differentiate into neurons, oligodendrocytes, and astrocytes. Chemically defined conditions are presented that enable a large number of neurons, up to 50% of the expanded cells, to be derived from the stem cells. In addition, four factors—PDGF, CNTF, LIF, and T3—have been identified which, individually, generate significantly higher proportions of neurons, astrocytes, or oligodendrocytes. These defined procedures permit a large—scale preparation of the mammalian CNS stem cells, neurons, astrocytes, and oligodendrocytes under chemically defined conditions with efficiency and control. These cells should be an important tool for many cell— and gene—based therapies for neurological disorders.

16 Claims, 46 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 11

Full	Title	Citation Front Review Classification Date Reference
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	00	Degrament ID: 110 5600602 A

☐ 90. Document ID: US 5688692 A

L21: Entry 90 of 93

File: USPT

Nov 18, 1997

US-PAT-NO: 5688692

DOCUMENT-IDENTIFIER: US 5688692 A

\*\* See image for Certificate of Correction \*\*

TITLE: Transgenic mouse cells expressing ts SV40 large T

DATE-ISSUED: November 18, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Jat; Parmjit Singh London GB2

Kioussis; Dimitris London GB2

Noble; Mark David Berkhamstead GB2

US-CL-CURRENT: 435/354; 435/325, 435/377, 435/69.1

#### ABSTRACT:

The provision of cell lines from virtually any cell type of the animal body is greatly facilitated by transgenic non-human eukaryotic animals of the invention in which at least some cells have (i) a differentiation inhibiting sequence chromosomally incorporated under the control of a non-constitutive promotor and/or (ii) a differentiation inhibiting sequence which is itself conditionally active. Said genes are chromosomally incorporated under the control of a promotor such that expression of said sequence is normally held below an effective level, thus allowing normal cell development. However, cells taken from said animal may be prevented from completing differentiation to a non-dividing state in tissue culture by activating expression of said sequence.

18 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full	Title Citation Front	Review Classification	Date Reference		Claims KMC Draw, Desi
		i			
	<del>,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,</del>		<del></del>		
	91. Document II	D: US 5672499 A			
L21:	Entry 91 of 93		File:	USPT	Sep 30, 1997

US-PAT-NO: 5672499

DOCUMENT-IDENTIFIER: US 5672499 A

TITLE: Immoralized neural crest stem cells and methods of making

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

NAME.

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

CA

Stemple; Derek L.

Newton

MA

US-CL-CURRENT: 435/353; 435/320.1, 435/325, 435/368, 435/467, 435/69.1

#### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

8 Claims, 62 Drawing figures Exemplary Claim Number: 1,2 Number of Drawing Sheets: 23 Full Title Citation Front Review Classification Date Reference Claims KAMC

☐ 92. Document ID: US 5654183 A

L21: Entry 92 of 93

File: USPT

Aug 5, 1997

US-PAT-NO: 5654183

DOCUMENT-IDENTIFIER: US 5654183 A

TITLE: Genetically engineered mammalian neural crest stem cells

DATE-ISSUED: August 5, 1997

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

CA

Stemple; Derek L.

Newton

MA

US-CL-CURRENT: 435/456; 435/320.1, 435/325, 435/353, 435/368, 435/69.1

## ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

17 Claims, 62 Drawing figures Exemplary Claim Number: 1,4 Number of Drawing Sheets: 23

Full Title Citation Front Review Classification Date Reference

Claims KMC Draw Desc

☐ 93. Document ID: US 5589376 A

L21: Entry 93 of 93

File: USPT

Dec 31, 1996

US-PAT-NO: 5589376

DOCUMENT-IDENTIFIER: US 5589376 A

TITLE: Mammalian neural crest stem cells

DATE-ISSUED: December 31, 1996

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J. Stemple; Derek L.

Altadena

Pasadena

CA

CA

US-CL-CURRENT: 435/325; 435/350, 435/351, 435/353, 435/363, 435/368

#### ABSTRACT:

The invention includes methods for the isolation and clonal propagation of mammalian neural crest stem cells and isolated cellular compositions comprising the same. The methods employ a novel separation and culturing regimen and bioassays for establishing the generation of neural crest stem cell derivatives. These methods result in the production of non-transformed neural crest stem cells and their progeny. The invention demonstrates, at the clonal level, the self regeneration and asymmetrical division of mammalian neural crest stem cells for the first time in feeder cell-independent cultures. Lineage restriction is demonstrated within a developing clone and is shown to be sensitive to the local environment. Neural crest stem cells cultured on a mixed substrate of poly-D-lysine and fibronectin generate PNS neurons and glia, but on fibronectin alone the stem cells generate PNS glia but not neurons. The neurogenic potential of the stem cells, while not expressed, is maintained over time on fibronectin. The invention further includes transplantation assays which allow for the identification of mammalian neural crest stem cells from various tissues. It also includes methods for transplanting mammalian neural crest stem cells and/or neural or glial progenitors into mammals.

10 Claims, 48 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 16

Full	Title Citation	Front Review	Classification	Date	Reference		Claims	KWMC Dr.	aw. Des
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# **Hit List**

Clear Generate Collection Print Fwd Refs Bkwd Refs Generate OACS

**Search Results -** Record(s) 1 through 100 of 189 returned.

☐ 1. Document ID: US 20040197317 A1

Using default format because multiple data bases are involved.

L26: Entry 1 of 189

File: PGPB

Oct 7, 2004

PGPUB-DOCUMENT-NUMBER: 20040197317

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040197317 A1

TITLE: Persistent expression of candidate molecule in proliferating stem and progenitor cells for delivery of therapeutic products

PUBLICATION-DATE: October 7, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

RULE-47

Rao, Mahendra S.

Capecchi, Mario R.

Timonium

Salt Lake City

MD US

COUNTRY

UT US

US-CL-CURRENT: 424/93.21; 435/366, 435/455

Full Title	Citation Front	Review	Classification	Date	Reference	Sequences	Claims	
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☐ 2. Document ID: US 20040187172 A1

L26: Entry 2 of 189

File: PGPB

Sep 23, 2004

PGPUB-DOCUMENT-NUMBER: 20040187172

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040187172 A1

TITLE: Transgenic animal for screening therapeutic agents for brain tumors

PUBLICATION-DATE: September 23, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Chiu, Ing-Ming

Dublin

OH

US

US-CL-CURRENT: 800/18

ABSTRACT:

A transgenic, non-human mammal useful for assessing the effect of candidate chemotherapeutic drugs on the growth of brain tumors in vivo is provided. Incorporated into the genome of the transgenic mammal, which preferably is a rodent,

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

is a transgene which comprises a promoter comprising the nuclear factor binding region of the RR2 cis acting element of a fibroblast growth factor 1B (FGF1B) promoter. Operably linked to the promoter is reporter gene comprising a sequence which encodes the SV40 large T antigen. A transgenic, non-human mammal useful for identifying and isolating FGF1 producing brain cells. Incorporated into the genome of these transgenic animals is a transgene which comprises a promoter comprising the nuclear factor binding region of the RR2 cis acting element of an fibroblast growth factor 1B (FGF1B) promoter. Operably linked to the promoter is reporter gene comprising a sequence which encodes a protein or polypeptide other than an SV40 large T antigen. A method of obtaining neural stem cells from a sample of cells obtained from an animal is also provided. Such method comprises introducing the FGF1B-detector transgene into a sample of cells that have been obtained from the animal, and assaying for expression of the detectable marker in the cells, wherein cells that express the marker are neural stem cells. The cells which express the detectable marker can then be isolated from the population to provide a sub-population of neural stem cells.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | KMC | Draw Description | Attachments | Claims | Claims | KMC | Draw Description | Attachments | Claims 
PGPUB-DOCUMENT-NUMBER: 20040161419

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040161419 A1

TITLE: Placental stem cells and uses thereof

PUBLICATION-DATE: August 19, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Strom, Stephen C. Allison Park PA US Miki, Toshio Pittsburgh PA US

US-CL-CURRENT: 424/93.21; 435/366

## ABSTRACT:

The present invention features novel placental stem cells and provides methods and compositions for the therapeutic uses of placental stem cells or placental stem cells that have been induced to differentiate into a desired tissue type into a recipient host in amounts sufficient to result in production of the desired cell type, e.g, hepatocytes, neural cells, pancreatic cells, vascular endothelial cells, cardiomyocytes.

Full Title Citation Front Review Clas	sification Date Reference Sequences Attach	iments   Claims   KWIC   Draw. Desc
☐ 4. Document ID: US 20040	152189 A1	
L26: Entry 4 of 189	File: PGPB	Aug 5, 2004

PGPUB-DOCUMENT-NUMBER: 20040152189

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040152189 A1

TITLE: Selective antibody targeting of undifferentiated stem cells

PUBLICATION-DATE: August 5, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

McWhir, Jim Midlothian CA GB CA Gold, Joseph D. San Francisco US

Schiff, J. Michael Menlo Park US

US-CL-CURRENT: 435/366; 435/455

## ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in expression of a cell-surface antigen that can be used to deplete the undifferentiated cells. Model effector sequences encode glycosyl transferases that synthesize carbohydrate xenoantigen or alloantigen, which can be used for immunoseparation or as a target for complement-mediated lysis. The differentiated cell populations produced are suitable for use in tissue regeneration and non-therapeutic applications such as drug screening.

Full   Title   Citation   Front   Review   Classificatio	n   Date   Reference   Sequences	Attachments   Claims   KMC   Draw Des
☐ 5. Document ID: US 2004014198		anarananananananananananananananananana
L26: Entry 5 of 189	File: PGPB	Jul 22, 2004

PGPUB-DOCUMENT-NUMBER: 20040141981

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040141981 A1

TITLE: Diagnosis and treatment of neuroectodermal tumors

PUBLICATION-DATE: July 22, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Sontheimer, Harald W. Birmingham ALUS Lyons, Susan A. Monterallo ALUS

US-CL-CURRENT: 424/178.1

#### ABSTRACT:

The present invention provides fusion proteins for the detection and treatment of neuroectodermal tumors. Previous work demonstrated that chlorotoxin is specific for glial-derived or meningioma-derived tumor cells. The current invention has extended the use of chlorotoxin-cytotoxin fusion proteins to treat the whole class neuroectodermal tumors such as gliomas, meningiomas, ependymonas, medulloblastomas, neuroblastomas, gangliomas, pheochromocytomas, melanomas, PPNET's, small cell carcinoma of the lung, Ewing's sarcoma, and metastatic tumors in the brain. Also, diagnostic methods are provided for screening neoplastic neuroectodermal tumors.

Full Title Citation Front Review Classification Date	Reference	Sequences	Attachments C	laims KMMC	Draw Desi
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☐ 6. Document ID: US 20040141946 A1					
L26: Entry 6 of 189	File:	PGPB		Jul 22,	2004

PGPUB-DOCUMENT-NUMBER: 20040141946

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040141946 A1

TITLE: Methods of treating neurological conditions with hematopoietic growth factors

PUBLICATION-DATE: July 22, 2004

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Schaebitz, Wolf-Ruediger	Dossenheim		DE	
Schneider, Armin	Heidelberg		DE	
Krueger, Carola	Speyer		DE	
Sommer, Clemens	Guenzburg		DE	
Schwab, Stefan	Heidelberg		DE	
Kollmar, Rainer	Heidelberg		DE	
Maurer, Martin	Heidelberg		DE	
Weber, Daniela	Mannheim		DE	
Gassler, Nikolaus	Heidelberg		DE	

US-CL-CURRENT:  $\underline{424}/\underline{85.1}$ ;  $\underline{424}/\underline{85.2}$ ,  $\underline{514}/\underline{12}$ 

## ABSTRACT:

The present invention relates to a method of treating neurological conditions in a mammal by administering a hematopoietic growth factor such as granulocyte-colony stimulating factor (GCSF) and granulocyte-macrophage colony stimulating factor (GMCSF). The invention also provides methods of screening for compounds that bind to a GCSF or GMCSF receptor found on the surface of a neuronal cell; and which provides a neuroprotective, neuroproliferative and/or a STAT gene activation activity.

Full Title Citation Front Review Classification Date	Reference   Sequences   Attach	ments Claims ΚΜΟ Dravu Desc
☐ 7. Document ID: US 20040137535 A1		
L26: Entry 7 of 189	File: PGPB	Jul 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040137535

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040137535 A1

TITLE: Enriched central nervous system stem cell and progenitor cell populations, and methods for identifying, isolating and enriching for such populations

PUBLICATION-DATE: July 15, 2004

INVENTOR-INFORMATION:

NAME STATE RULE-47 CITY COUNTRY

Uchida, Nobuko Palo Alto CA US Mountain View CA US Capela, Alexandra

US-CL-CURRENT: 435/7.2; 435/368

#### ABSTRACT:

Enriched neural stem and progenitor cell populations, and methods for identifying, isolating and enriching for neural stem cells using reagents that bind to cell surface markers are provided.

Full	Title Citation Front	Review   Classification   Da	ite Reference	Sequences	Attachments	Claims	KWIC	Drawt Des
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	8. Document ID:	US 20040121460 A	1					
L26:	Entry 8 of 189		File:	PGPB		Jun	24,	2004

PGPUB-DOCUMENT-NUMBER: 20040121460

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040121460 A1

TITLE: Differentiation of stem cells to pancreatic endocrine cells

PUBLICATION-DATE: June 24, 2004

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lumelsky, Nadya L	Washington	DC	US	
Blondel, Oliver	Bethesda	MD	US	
McKay, Ronald D	Bethesda	MD	US	
Kim, Jong-Hoon	Rockville	MD <sup>,</sup>	US	

US-CL-CURRENT: 435/366; 435/354

## ABSTRACT:

A method is provided for differentiating embryonic stem cells to endocrine cells. The method includes generating embryoid bodies from a culture of undifferentiated embryonic stem cells, selecting endocrine precursor cells, expanding the endocrine precursor cells by culturing endocrine cells in an expansion medium that comprises a growth factor, and differentiating the expanded endocrine precursor cells in a differentiation media to differentiated endocrine cells produced by this method are also provided. Artificial islets are disclosed, as well as method for using the pancreatic endocrine cells and the artificial islets.

Full	Titl∈	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Draw: Desc

☐ 9. Document ID: US 20040115175 A1

L26: Entry 9 of 189

File: PGPB

Jun 17, 2004

PGPUB-DOCUMENT-NUMBER: 20040115175

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040115175 A1

TITLE: Methods for treating disorders of neuronal deficiency with bone marrow-derived

cells

PUBLICATION-DATE: June 17, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Blau, Helen M. Menlo Park US Brazelton, Timothy Cupertino CA US Weimann, James M. Palo Alto CA US

US-CL-CURRENT: 424/93.7

#### ABSTRACT:

The invention provides, among other things, novel methods of treating neurological disorders which result in the loss of neurons (neuronal deficiencies). Bone marrow-derived cells are administered to individuals suffering from neuronal deficiencies. Administration of bone marrow-derived cells results in formation of bone marrow derived neurons, whether formed de novo or as a result of fusion with an existing neuron, thereby replacing or repairing lost or damaged neurons. The methods of the invention may also be used for memory augmentation in memory impaired individuals.

Full Title Citation Front Review Classification	n Date Reference Sequences Attac	chments Claims KMC Draw Desc
☐ 10. Document ID: US 200401074	453 A1	
L26: Entry 10 of 189	File: PGPB	Jun 3, 2004

PGPUB-DOCUMENT-NUMBER: 20040107453

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040107453 A1

TITLE: Multipotent adult stem cells, sources thereof, methods of obtaining same, methods of differentiation thereof, methods of use thereof and cells derived thereof

PUBLICATION-DATE: June 3, 2004

INVENTOR-INFORMATION:

CITY NAME STATE COUNTRY RULE-47 Furcht, Leo T Minneapolis US Verfaillie, catherine M St Paul MN US Reyes, Morayma Minneapolis MN US

US-CL-CURRENT: 800/18; 424/93.7, 435/353, 435/354, 435/366, 800/21

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#### ABSTRACT:

The present invention relates generally to mammalian multipotent adult stem cells (MASC), and more specifically to methods for obtaining, maintaining and differentiating MASC to cells of multiple tissue types. Uses of MASC in the therapeutic treatment of disease are also provided.

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Full	Title Citatio	on Front	Review	Classification	Date	Reference S	Sequences	Attachments	Claims	KWIC	Drawi Desc
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	11. Doci	ument ID	): US 2	004010584	7 A l						
L26:	Entry 11	of 189				File:	PGPB		Ju	n 3,	2004

PGPUB-DOCUMENT-NUMBER: 20040105847

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040105847 A1

TITLE: Promoting Recovery from Damage to the Central Nervous System

PUBLICATION-DATE: June 3, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Finklestein, Seth P. Needham MA US Snyder, Evan Y. Jamaica Plain MA US

US-CL-CURRENT: 424/93.7; 514/12

#### ABSTRACT:

Methods, kits and compositions for improving a subject's recovery from CNS injury are disclosed. In certain aspects, a method may include administering to a subject cells and a neural stimulant. Recovery may be manifest by improvements in sensorimotor or cognitive abilities, e.g., improved limb movement and control or improved speech capability. In certain embodiments, subject methods can be used as part of a treatment for damage resulting from ischemia, hypoxia or trauma.

Full Title Citation Front Review Classification	Date Reference Sequences Atta	chments Claims KWC Draw Desc
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☐ 12. Document ID: US 2004010344	18 A1	
L26: Entry 12 of 189	File: PGPB	May 27, 2004

PGPUB-DOCUMENT-NUMBER: 20040103448

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040103448 A1

TITLE: Methods for inducing in vivo proliferation and migration of transplanted progenitor cells in the brain

PUBLICATION-DATE: May 27, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Bjorklund, Anders

Lund

SE

US-CL-CURRENT: 800/9; 435/368

#### ABSTRACT:

The present invention provides methods of inducing in vivo migration and proliferation of progenitor cells transplanted to the brain. Isolation, characterization, proliferation, differentiation and transplantation of mammalian neural stem cells are also disclosed.

Full	Title Citation Front Review	Classification Date	Reference	Sequences	Attachments	Claims	KWAC	Draw, Desi
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	13. Document ID: US 20	0040092013 A1						
L26:	Entry 13 of 189	,	File:	PGPB		Мау	13,	2004

PGPUB-DOCUMENT-NUMBER: 20040092013

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040092013 A1

TITLE: Method of treating alzheimer's disease with cell therapy

PUBLICATION-DATE: May 13, 2004

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Snyder, Evan Y.	La Jolla	CA	US	
Loring, Jeanne F.	Del Mar	CA	US	
Snable, Gary L.	Atherton	CA	US	
Aboody, Karen S.	Arcadia	CA	US	
Daadi, Marcel M.	Palo Alto	CA	US	

US-CL-CURRENT: 435/368; 424/93.7

#### ABSTRACT:

A method of treating Alzheimer's disease provides for administering NSC to a susceptible individual. Preferably the NSCs are administered intracisternally. Other administration routes are spinal injection, ventricular injection or systemic injection. Preferably, the quantity of NSC administered is in a range of about 400,000 to about 40,000,000. More preferably, the quantity of NSC is about 1,000,000 to about 10,000,000. The NSCs are administered at multiple locations. The NSCs can be administered to the neocortex or other affected areas of both hemispheres. The method of preventing further deterioration in cognitive function in a person diagnosed with Alzheimer's disease provides for administering NSC to the person in sufficient quantity to prevent additional loss of cognitive function.

Cull	Title	Chation	Feart	Pavisor	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desi
F 12 II	IIII	Citation	FIGURE	17 5 415 44	018221110811011							

L26: Entry 14 of 189 File: PGPB May 13, 2004

PGPUB-DOCUMENT-NUMBER: 20040092010

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040092010 A1

TITLE: Method of proliferating and inducing brain stem cells to differentiate to

neurons

PUBLICATION-DATE: May 13, 2004

INVENTOR-INFORMATION:

CITY	STATE	COUNTRY	RULE-47
New York	NY	US .	
San Francisco	CA	US	
San Francisco	CA	US	
Marseille	NY	FR	
New York	*	ŲS	
	New York San Francisco San Francisco Marseille	New York NY San Francisco CA San Francisco CA Marseille NY	New York NY US San Francisco CA US San Francisco CA US Marseille NY FR

US-CL-CURRENT: 435/354; 435/368

#### ABSTRACT:

The present invention discloses methods of producing neuronal cells from stem cells, particularly from adult brain stem cells. The use of such neuronal cells in the treatment and/or prevention of neurological diseases, conditions and/or injuries is also disclosed. In addition, the present invention provides a novel source of neuronal cells for use as a laboratory tool.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments	Claims	KWAC	Draw, Desc
☐ 15. Document ID: US 20040072345 A1		!			
L26: Entry 15 of 189	File: PGPB		Apı	15,	2004

PGPUB-DOCUMENT-NUMBER: 20040072345

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040072345 A1

TITLE: Method and compositions for inhibiting tumorigenesis

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Altaba, Ariel Ruiz i. New York NY US
Sanchez, Maria Pilar New York NY US

US-CL-CURRENT: 435/368; 435/354

# ABSTRACT:

The present invention discloses methods of producing neuronal cells from stem cells, particularly from adult brain stem cells. The use of such neuronal cells in the

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treatment and/or prevention of neurological diseases, conditions and/or injuries is also disclosed. In addition, the present invention provides a novel source of neuronal cells for use as a laboratory tool.

Full	Title	Citation   Front	Review Classification	Date (	Reference	Sequences	Attachments	Claims	KWAC	Draw, Desc
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	16.	Document ID	: US 20040072344	4 A1						
L26:	Entr	y 16 of 189			File:	PGPB		Apr	15,	2004

PGPUB-DOCUMENT-NUMBER: 20040072344

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040072344 A1

TITLE: Method for inducing differentiation of embryonic stem cells into functioning

cells

PUBLICATION-DATE: April 15, 2004

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Inoue, Kazutomo	Kyoto-shi		JP	
Kim, Dohoon	Kyoto-shi		JP	
Gu, Yanjun	Kyoto-shi		JP	
Ishii, Michiyo	Kyoto-shi		JP	

US-CL-CURRENT: 435/366

#### ABSTRACT:

The present invention provides a 4-step method for inducing differentiation of embryonic stem cells into functioning cells comprising 1) expanding ES cells; 2) inducing Embryoid Bodies in the presence of leukemia inhibitory factor and <u>basic FGF</u>; 3) selection expanding of the EBs and 4) differentiation. According to the present invention, ES cells can be differentiated into either insulin producing pancreatic islet like cell clusters or nerve like cells. Thus obtained functioning cells may be potential sources of donor cells in cell transplant therapy for many patients.

ĺ	Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Draw, Desi
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		17.	Docum	ent ID	): US 2	004007166	55 A1						
	L26:	Entr	y 17 of	189				File:	PGPB		Apr	15,	2004

PGPUB-DOCUMENT-NUMBER: 20040071665

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040071665 A1

TITLE: Method for therapeutically treating a clinically recognized form of

cardiopathology in a living mammal

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Xiao, Yong-Fu

Wayland

MA

US

Morgan, James P.

Newton Centre

MA

US

US-CL-CURRENT: 424/93.7

## ABSTRACT:

The present invention provides therapeutic methods which employ one or more identifiable types of mammalian stem cells, and/or their progenitor progeny cells, and/or their lineage-committed descendant cells, and/or their partiallydifferentiated offspring cells--with or without completely differentiated cells--to treat living mammalian subjects afflicted with a clinically recognized form of cardiopathology. The identifiable cell types include embryonic stem cells and their offspring cells; as well as the presently identified types of adult stem cells and their various offspring cells; and also include recently identified alternative cell types which have functional stem cell properties. Among the clinical forms of cardiopathology which can be efficaciously treated using the present therapeutic methods are myocardial infarction, myocarditis, heart failure, and cardiac dysrhythmia.

Full	Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWAC	Draw, Desi
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	18.	Document ID	): US 2	004006320	2 A1						

PGPUB-DOCUMENT-NUMBER: 20040063202 PGPUB-FILING-TYPE: new

L26: Entry 18 of 189

DOCUMENT-IDENTIFIER: US 20040063202 A1

TITLE: Neurogenesis from hepatic stem cells

PUBLICATION-DATE: April 1, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

File: PGPB

COUNTRY

RULE-47

Apr 1, 2004

Petersen, Bryon E.

Gainesville Gainesville FL FL US

US-CL-CURRENT: 435/368

#### ABSTRACT:

Deng, Jie

In vitro and in vivo approaches were used to induce hepatic oval cells to differentiate into cells expressing a neural cell-specific marker and displaying a neural morphology. Increasing cAMP in hepatic oval cells or co-culturing hepatic oval cells with neurospheres caused the hepatic oval cells to develop into cells displaying a neural cell-like phenotype. Hepatic oval cells transplanted into a brain differentiated into cells that phenotypically resembled all of the major cell types in the brain, including astrocytes, neurons, and microglia.

☐ 19. Document ID: US 20040048373 A1

L26: Entry 19 of 189

File: PGPB

\_ Mar 11, 2004

PGPUB-DOCUMENT-NUMBER: 20040048373

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040048373 A1

TITLE: Method for production of neuroblasts

PUBLICATION-DATE: March 11, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Gage, Fred H. La Jolla CA US
Ray, Jasodhara San Diego CA US

US-CL-CURRENT: 435/368

#### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Draw, Desi	
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	20.	Docum	ent ID	: US 2	004003359	7 A l	-						
T-26.	Entr	y 20 of	189				File:	PGPB		Feb	19.	2004	

PGPUB-DOCUMENT-NUMBER: 20040033597

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040033597 A1

TITLE: Multipotent neural stemcells from peripheral tissues and uses thereof

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Toronto Ontario		CA	
Akhavan, Mahnaz	Toronto Ontario		CA	
Fernandes, Karl J. L.	Toronto Ontario		CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Toronto Ontario		CA	
Golster, Andrew	Saskatoon Sakatchewan		CA	

US-CL-CURRENT: 435/368; 435/371

#### ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Full Title	Citation Front	Review Classifica	ion Date Referenc	e Sequences /	Attachments Claims	KMC Draw Desi
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☐ 21. Document ID: US 20040029269 A1

L26: Entry 21 of 189

File: PGPB

Feb 12, 2004

PGPUB-DOCUMENT-NUMBER: 20040029269

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040029269 A1

TITLE: Promoter-based isolation, purification, expansion, and transplantation of neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells from a population of embryonic stem cells

PUBLICATION-DATE: February 12, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Goldman, Steven A. South Salem NY US
Roy, Neeta Singh New York NY US

US-CL-CURRENT: 435/368

## ABSTRACT:

The present invention relates to a method of isolating neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells from a population of embryonic stem cells. This method comprises selecting a promoter which functions only in neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells and introducing a nucleic acid molecule encoding a marker protein under control of said promoter into the population of embryonic stem cells. The population of embryonic stem cells are then differentiated to produce a mixed population of cells comprising neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells. The neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells are then allowed to express the marker protein. Cells expressing the marker protein are separated from the mixed population of cells, where the separated cells are neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells. In an alternative embodiment, the embryonic stem cells are differentiated before the nucleic acid is introduced. The present invention also relates to the resulting neuronal progenitor cells, oligodendrocyte progenitor cells, or neural stem cells themselves.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Drawi Desi
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☐ 22. Document ID: US 20040009593 A1

L26: Entry 22 of 189 File: PGPB Jan 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040009593

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040009593 A1

TITLE: Oligodendrocytes derived from human embryonic stem cells for remyelination and

treatment of spinal cord injury

PUBLICATION-DATE: January 15, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Keirstead, Hans S. Irvine CA US Nistor, Gabriel I. Placentia CA US

US-CL-CURRENT: 435/368

#### ABSTRACT:

This invention provides populations of neural cells bearing markers of glial cells, such as oligodendrocytes and their precursors. The populations are generated by differentiating pluripotent stem cells such as human embryonic stem cells under conditions that promote enrichment of cells with the desired phenotype or functional capability. Various combinations of differentiation factors and mitogens can be used to produce cell populations that are over 95% homogeneous in morphological appearance, and the expression of oligodendrocyte markers such as GalC. The cells are capable of forming myelin sheaths, and can be used therapeutically improve function of the central nervous system.

Full Title Citation Front Revie	oo Classification Date Ro	eference Sequences A	Attachments Claims K	MC Draw Desi

## ☐ 23. Document ID: US 20040009592 A1

L26: Entry 23 of 189 File: PGPB Jan 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040009592

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040009592 A1

TITLE: Genetically-modified neural progenitors and uses thereof

PUBLICATION-DATE: January 15, 2004

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Sabate, Olivier FR Paris FR Horellou, Philippe Paris Buc-Caron, Marie-Helene Paris FR Mallet, Jacques Paris FR

US-CL-CURRENT: 435/368

ABSTRACT:

The invention concerns human neural progenitor cells containing introduced genetic material encoding a product of interest, and their use for the treatment of neurodegenerative diseases.

Full	Title Citation Front Review Classification Dat	e Reference S	equences	Attachments	Claims	KMAC	Draw Desc
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	24. Document ID: US 20040005704 A	1					
T.26:	Entry 24 of 189	File:	PGPB		Ja	n 8.	2004
<b></b> .	1					,	

PGPUB-DOCUMENT-NUMBER: 20040005704

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040005704 A1

TITLE: Low oxygen culturing of central nervous system progenitor cells

PUBLICATION-DATE: January 8, 2004

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Csete, Marie	Ann Arbor	MI	US	
Doyle, John	South Pasadena	CA	US	
Wold, Barbara J.	San Marino	CA	US	
McKay, Ron	Bethesda	MD	US	
Studer, Lorenz	New York	NY	US	

US-CL-CURRENT: 435/368

#### ABSTRACT:

The present invention relates to the growth of cells in culture under conditions that promote cell survival, proliferation, and/or cellular differentiation. The present inventors have found that proliferation was promoted and apoptosis reduced when cells were grown in lowered oxygen as compared to environmental oxygen conditions traditionally employed in cell culture techniques. Further, the inventors found that differentiation of precursor cells to specific fates also was enhanced in lowered oxygen where a much greater number and fraction of dopaminergic neurons were obtained when mesencephalic precursors were expanded and differentiated in lowered oxygen conditions. Thus at more physiological oxygen levels the proliferation and differentiation of CNS precursors is enhanced, and lowered oxygen is a useful adjunct for ex vivo generation of specific neuron types. Methods and compositions exploiting these findings are described.

Full Title Citation Front Review Classificati	ion Date Reference Sequences Attacl	nments Claims KWMC Draw. Desc
		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
☐ 25. Document ID: US 20040005	6661 A1	
L26: Entry 25 of 189	File: PGPB	Jan 8, 2004

PGPUB-DOCUMENT-NUMBER: 20040005661

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040005661 A1

TITLE: Potential growth factors from the human tumour cell line ht 1080

PUBLICATION-DATE: January 8, 2004

INVENTOR~INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Minger, Stephen L. London GB Adams, Gregor London GB Francis, Paul London GB London Mcclure, Myra GB

US-CL-CURRENT: 435/69.1; 435/226, 435/320.1, 435/366, 530/350, 536/23.2

#### ABSTRACT:

The invention relates to a mitogen obtainable from a human tumour cell line, such as from HT1080 cells.

Full	Title	Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Desc
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	26	Dayward ID. 115 20020226150 A1

☐ 26. Document ID: US 20030226159 A1

L26: Entry 26 of 189

File: PGPB

Dec 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030226159

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030226159 A1

TITLE: Cancer models

PUBLICATION-DATE: December 4, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Bachoo, Robert M. Roslindale US MA

Depinho, Ronald A. Brookline MΑ US

US-CL-CURRENT: 800/18; 435/354

#### ABSTRACT:

The invention provides chimeric non-human animals, methods for making and using chimeric non-human animals, isolated stem cells, and methods for identifying agents that reduces cancer in a non-human animal. For example, the invention relates to using stem cells to make chimeric non-human animals having cancer or the ability to develop cancer. Such animals can be used to evaluate tumorigenesis, tumor maintenance, and tumor regression in vivo. In addition, the chimeric non-human animals provided herein can be used to identify agents that reduce or prevent tumor formation or growth in vivo.

Full Title Citation Front Review	Classification Date Reference	e Sequences Attachments Claims KMC Draw D	e <b>≾</b> i

# ☐ 27. Document ID: US 20030211603 A1

L26: Entry 27 of 189

File: PGPB

Nov 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030211603

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030211603 A1

TITLE: Reprogramming cells for enhanced differentiation capacity using pluripotent stem cells

PUBLICATION-DATE: November 13, 2003

#### TNVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Earp, David J.	Oakland	CA	US	
Carpenter, Melissa K.	Castro Valley	CA	US	
Gold, Joseph D.	San Francisco	CA	US	
Lebkowski, Jane S.	Portola Valley	CA	US	
Schiff, J. Michael	Menlo Park	CA	US .	

US-CL-CURRENT: 435/366

#### ABSTRACT:

Described in this disclosure is a new process whereby cells of one tissue type can be reprogrammed to produce cells of a different tissue type. Cells from a human donor are reprogrammed by culturing adjacent to primate pluripotent stem cells (in an undifferentiated or newly differentiated state) or in an environment supplemented by components taken from pPS cells. Simultaneously or in a subsequent step, the donor cells can be treated in a manner that enhances differentiation towards a different tissue type. In this manner, patients in need of tissue regeneration can be treated with cells differentiated and reprogrammed from their own autologous cell donation.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Desc												
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E 518	11(1)	CHEIDH:	F 113111	17 G 0 (G00	Classingarion	Date	Melelelion	Sednetices	Curae Illiette	STATIS :	KOOLC D	16-000-684-680

## ☐ 28. Document ID: US 20030211087 A1

L26: Entry 28 of 189

File: PGPB

Nov 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030211087

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030211087 A1

TITLE: Neutral progenitor cells from hippocampal tissue and a method for isolating

and purifying them

PUBLICATION-DATE: November 13, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Goldman, Steven A. South Salem NY US

US-CL-CURRENT: 424/93.21; 435/368, 435/456

### ABSTRACT:

The present invention relates to an enriched or purified preparation of isolated hippocampal neural progenitor cells and progeny thereof. The present invention also relates to a method of separating neural progenitor cells from a mixed population of cell types from hippocampal tissue. This method includes selecting a promoter which functions selectively in the neural progenitor cells, introducing a nucleic acid molecule encoding a fluorescent protein under control of said promoter into all cell types of the mixed population of cell types from hippocampal tissue, allowing only the neural progenitor cells, but not other cell types, within the mixed population to express said fluorescent protein, identifying cells of the mixed population of cell types that are fluorescent, which are restricted to the neural progenitor cells, and separating the fluorescent cells from the mixed population of cell types, wherein the separated cells are restricted to the neural progenitor cells.

Full	Title Citation Front Review	Classification Date	Reference S	Sequences	Attachments	Claims	KWIC	Drawi Desc
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	29. Document ID: US	20030207450 A1						
L26:	Entry 29 of 189		File:	PGPB		No	v 6,	2003

PGPUB-DOCUMENT-NUMBER: 20030207450

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030207450 A1

TITLE: Isolation and transplantation of retinal stem cells

PUBLICATION-DATE: November 6, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Young, Michael J.	Gloucester	MA	US	
Klassen, Henry J.	Pasadena	CA	US	
Shatos, Marie A.	Athol	MA	US	
Mizumoto, Keiko	Higashi		JP	

US-CL-CURRENT: 435/368

### ABSTRACT:

The present invention relates to the isolation, in vitro propagation, and transplantation and integration of non-pigmented retinal stem cells derived from the neuroretina of the eye, ex vivo and in vivo.

Full	Title	Citation Front	Review Classification	Date	Reference	Sequences	Attachments	Claims	KWMC	Draw, Desc
			US 2003020336							
T.26.		v 30 of 189			File:	PGPB,		. Oct	30.	2003

PGPUB-DOCUMENT-NUMBER: 20030203361

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030203361 A1

TITLE: 13 human colon and colon cancer associated proteins

PUBLICATION-DATE: October 30, 2003

INVENTOR-INFORMATION:

STATE RULE-47 CITY COUNTRY NAME

Rosen, Craig A. Laytonsville MD US Birse, Charles E. North Potomac MD US

US-CL-CURRENT: 435/6; 435/183, 435/320.1, 435/325, 435/69.3, 435/7.23, 536/23.2

### ABSTRACT:

This invention relates to newly identified colon or colon cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "colon or colon cancer antigens", and the use of such colon antigens for detecting disorders of the gastrointestinal system, particularly the presence of colon cancer and colon cancer metastases. This invention relates to colon or colon cancer antigens as well as vectors, host cells, antibodies directed to colon or colon cancer antigens and the recombinant methods and synthetic methods for producing the same. Also provided are diagnostic methods for detecting, treating, preventing and/or prognosing disorders related to the colon, including colon cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of colon or colon cancer antigens of the invention. The present invention further relates to inhibiting the production and function of the polypeptides of the present invention.

Full	1	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWAC	Draw Desc
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Oct 23, 2003 L26: Entry 31 of 189 File: PGPB

PGPUB-DOCUMENT-NUMBER: 20030199447

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030199447 A1

TITLE: Enhancing neurotrophin-induced neurogenesis by endogenous neural progenitor cells by concurrent overexpression of brain derived neurotrophic factor and an inhibitor of a pro-gliogenic bone morphogenetic protein

PUBLICATION-DATE: October 23, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Goldman, Steven A.	South Salem	NY	US	
Chmielnicki, Eva	New York	NY	US	
Economides, Aris	Tarrytown	NY	US	

US-CL-CURRENT: 514/12; 424/93.2, 514/44

# ABSTRACT:

The present invention relates to a method of inducing neuronal production in a subject, a method of recruiting neurons to a subject's brain, and a method of

treating a neurodegenerative condition by administering a neurotrophic factor and an inhibitor of pro-gliogenic bone morphogenetic proteins. Also disclosed is a method of suppressing astrocyte generation and inducing neuronal production in a subject, a method of treating a neurologic condition, and a method of suppressing glial scar formation in a subject by administering an inhibitor of pro-gliogenic bone morphogenetic proteins. Finally, the present invention involves a method of introducing a heterogeneous protein into a subject's brain and spinal cord by introducing a nucleic acid molecule encoding the heterogeneous protein introduced into the subject's ependyma, permitting the protein from the nucleic acid molecule to be expressed within the subject's ependyma, and permitting the expressed protein to migrate within the subject's brain and spinal cord.

Full   Title   Citation   Front   Review   Classification	Date Reference Sequences .	Attachments Claims KWC Draw Desc
☐ 32. Document ID: US 20030175954	Al	
L26: Entry 32 of 189	File: PGPB	Sep 18, 2003

PGPUB-DOCUMENT-NUMBER: 20030175954

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030175954 A1

TITLE: Human embryoid body-derived cells

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Shamblott, Michael J. Baltimore MD US Gearhart, John D. Baltimore MD US

US-CL-CURRENT: 435/366; 435/69.1

### ABSTRACT:

The invention is directed to novel cells that are derived from human embryoid bodies. Such embryoid body-derived (EBD) cells are relatively uncommitted or progenitor (e.g., pluripotent) cells. EBD cells, while not immortal, display long-term proliferation in culture with a normal karyotype and can be cryopreserved and cloned. They can be efficiently transfected with retroviruses and lentivirus and genetically manipulated. Although they have a developmentally broad multilineage expression profile, they do not form tumors when injected into severe combined immunodeficiency (SCID) mice. As a result, EBD cells have a variety of uses, for example, in transplantation therapies.

Full Title Citation Front Review Classification Date F	Reference   Sequences	Attachments   Claims   1	ONIC Draw. Des
☐ 33. Document ID: US 20030170736 A1	,		enna en
L26: Entry 33 of 189	File: PGPB	Sep	11, 2003

PGPUB-DOCUMENT-NUMBER: 20030170736

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030170736 A1

TITLE: Methods and compositions for producing neural progenitor cells

PUBLICATION-DATE: September 11, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Agoston, Denes V. Bethesda MD US

US-CL-CURRENT: 435/7.2; 435/368, 435/455, 530/388.26

#### ABSTRACT:

The invention relates generally to methods and compositions for altering the differentiation status of cells such as stem and progenitor cells, and producing these cells for transplantation into mammals. The differentiation status of cells can be altered by contacting a nucleic acid decoy molecule to a mammalian cells and culturing the cell, whereby the differentiation status of the cell is altered. Pharmaceutical compositions of the invention are capable of entering a cell and binding to a protein in the cell and thereby altering a septamer function, a septamer-downstream function or a septamer-related function. The methods disclosed herein can be used in treating diseases by providing new cells to ameliorate symptoms of the disorder. Preferably, methods of the invention create homogeneous populations of progenitor and other cells, that can be administered to patients by transplantation. Diseases and disorders that can be treated in this fashion include, but are not limited to, CNS disorders, disorders of the lymphatic system, endothelial cell disorders, epithelial cell disorders, erythropoietic and hematopoietic diseases and disorders, neuro-degenerative disease, and traumatic brain injuries.

Full Title Citation Front Review Classification	n Date Reference	Sequences Attachments	Claims KMC Draw Desc
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☐ 34. Document ID: US 200301662	76 A1		
L26: Entry 34 of 189	File	: PGPB	Sep 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030166276

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030166276 A1

TITLE: Cultures of human CNS neural stem cells

PUBLICATION-DATE: September 4, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Carpenter, Melissa Foster City CA US

US-CL-CURRENT: 435/368

### ABSTRACT:

The invention provides a cell culture including proliferating human neural stem cells with a doubling rate faster than thirty days. The invention also provides a cell culture media for proliferating mammalian neural cells including a standard defined culture medium, a carbohydrate source, a buffer, a source of hormones, one or more growth factors that stimulate the proliferation of neural stem cells, and LIF. The invention also provides a method for protecting, repairing or replacing damaged

tissue comprising transplanting mammalian neural stem cells formed into neurospheres. The invention also provides a cell culture of differentiated human neural stem cells where the cells are glioblasts. The invention also provides a method of differentiating human neural stem cells in culture media.

Full	Title Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desi

# ☐ 35. Document ID: US 20030162290 A1

L26: Entry 35 of 189

File: PGPB

Aug 28, 2003

PGPUB-DOCUMENT-NUMBER: 20030162290

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162290 A1

TITLE: Method for inducing differentiation of embryonic stem cells into functioning

cells

PUBLICATION-DATE: August 28, 2003

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Inoue, Kazutomo	Sakyo-ku		JP	
Kim, Dohoon	Sakyo-ku		JP	
Gu, Yanjun	Sakyo-ku		JP	
Ishii, Michiyo	Kamigyo-ku		JP	

US-CL-CURRENT: 435/366; 435/372

# ABSTRACT:

The present invention provides a 4-step method for inducing differentiation of embryonic stem cells into functioning cells comprising 1) expanding ES cells; 2) inducing Embryoid Bodies in the presence of leukemia Inhibitor factor and basic FGF; 3) selection expanding of the EBs and 4) differentiation. According to the present invention, ES cells can be differentiated into either insulin producing pancreatic islet like cell clusters or nerve like cells. Thus obtained functioning cells may be potential sources of donor cells in cell transplant therapy for many patients.

Full Title Citation Front Review Classification	on Date Reference Sequences A	ttachments Claims KWMC Draw Desi
☐ 36. Document ID: US 200301613	818 A1	
L26: Entry 36 of 189	File: PGPB	Aug 28, 2003

PGPUB-DOCUMENT-NUMBER: 20030161818

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030161818 A1

TITLE: Cultures, products and methods using stem cells

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Weiss, Mark L. KS Manhattan US Troyer, Deryl L. US Manhattan KS Davis, Duane Westmoreland KS US Mitchell, Kathy E. US Manhattan KS

US-CL-CURRENT: 424/93.21; 435/368, 435/372, 514/44

### ABSTRACT:

Stem cells from human sources can have a variety of useful applications in disease treatment and biotechnology. More particularly the umbilical cord matrix stem (UCMS) cell cultures of the invention have a variety of totipotent, pluriotent, or multipotent cells for a variety of end uses from a non-controversial, universally available, species-specific source. The technology can have application to any placental animal, including agricultural and laboratory animals and humans. The invention relates to isolating, culturing the stem cells, maintaining the stem cells, transforming the stem cells into useful cell types using genetic or other transformation technologies, stem cell and tissue banking and using untransformed or transformed cells in disease treatment.

Full	Title Citation Front Review Class	fication   Date   F	Reference Sequences	Attachments Claims	KWMC   Draw Desi
			·		
					·
	37. Document ID: US 20030	161817 A1		,	
L26:	Entry 37 of 189		File: PGPB	Aug	28, 2003

PGPUB-DOCUMENT-NUMBER: 20030161817

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030161817 A1

TITLE: Pluripotent embryonic-like stem cells, compositions, methods and uses thereof

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Young, Henry E. Macon GA US Lucas, Paul A. Poughkeepsie NY

US-CL-CURRENT: 424/93.21; 435/366

# ABSTRACT:

The present invention relates to pluripotent stem cells, particularly to pluripotent embryonic-like stem cells. The invention further relates to methods of purifying pluripotent embryonic-like stem cells and to compositions, cultures and clones thereof. The present invention also relates to a method of transplanting the pluripotent stem cells of the present invention in a mammalian host, such as human, comprising introducing the stem cells, into the host. The invention further relates to methods of in vivo administration of a protein or gene of interest comprising transfecting a pluripotent stem cell with a construct comprising DNA which encodes a protein of interest and them introducing the stem cell into the host where the protein or gene of interest is expressed. The present also relates to methods of

producing mesodermal, endodermal or ectodermal lineage-committed cells by culturing or transplantation of the pluripotent stem cells of the present invention.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw. Desc

☐ 38. Document ID: US 20030148514 A1

L26: Entry 38 of 189

File: PGPB

Aug 7, 2003

PGPUB-DOCUMENT-NUMBER: 20030148514

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030148514 A1

TITLE: Human embryonic germ cell line and methods of use

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Gearhart, John D. Baltimore MD US Shamblott, Michael Joseph Baltimore MD US

US-CL-CURRENT: 435/368

### ABSTRACT:

Primordial germ cells isolated from human embryonic tissue, such as from the gonadal ridges of human embryo, are disclosed. The primordial germ cells are cultured resulting in cells that resemble embryonic stem cells or embryonic germ cells in morphology and pluripotency. The cells are maintained several months in culture and can be genetically manipulated using transgenic technology to insert heterologous genetic material.

Fuli	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Drawi Desi
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File: PGPB

# ☐ 39. Document ID: US 20030147873 A1

L26: Entry 39 of 189

PGPUB-DOCUMENT-NUMBER: 20030147873

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030147873 A1

TITLE: Neural transplantation using pluripotent neuroepithelial cells

PUBLICATION-DATE: August 7, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Sinden, John London GB
Gray, Jeffrey A. London GB
Hodges, Helen London GB

Aug 7, 2003

Kershaw, Timothy Rashid-Doubell, Fiza London Oxford

GB

US-CL-CURRENT: 424/93.21; 435/368

ABSTRACT:

The subject invention pertains to a novel method of correction of behavioral and/or psychological deficits made possible by the intracerebral transplantation of pluripotent neuroepithelial cells. Cells, cell lines, pharmaceutical preparations, medicaments, methods for the production and maintenance of the cell lines for use in the method of the invention are encompassed by the invention.

Full	Title Citation Front	Review Classification (	Date   Reference	Sequences	Attachments	Claims	KWIC	Draw, Desc
	40. Document ID:	US 20030134413	<b>Å</b> 1					
L26:	Entry 40 of 189		File:	PGPB		Jul	17,	2003

PGPUB-DOCUMENT-NUMBER: 20030134413

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030134413 A1

TITLE: Cell production

PUBLICATION-DATE: July 17, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Rathjen, Peter David Mircham AU Rathjen, Joy Mircham AU

US-CL-CURRENT: 435/368

# ABSTRACT:

A method of producing neurectoderm cells, which method includes providing a source of early primitive ectoderm-like (EPL) cells; a conditioned medium as hereinbefore defined; or an extract therefrom exhibiting neural inducing properties; and contacting the EPL cells with the conditioned medium, for a time sufficient to generate controlled differentiation to neurectoderm cells.

Full Title Citation Front Review Classification Date	Reference Sec	quences Attachments	Claims Ki	04C	Draw, Des
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☐ 41. Document ID: US 20030118566 A1					
L26: Entry 41 of 189	File: PG	GPB	Jun 2	26,	2003

PGPUB-DOCUMENT-NUMBER: 20030118566

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030118566 A1

TITLE: Compositions and methods for isolation, propagation, and differentiation of

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

human stem cells and uses thereof

PUBLICATION-DATE: June 26, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Neuman, Toomas Santa Monica CA US Levesque, Michel Beverly Hills CA US

US-CL-CURRENT: 424/93.21; 424/93.7, 435/368

### ABSTRACT:

The invention is directed to the field of human stem cells and includes methods and compositions for isolating, propagating, and differentiating human stem cells. The invention provides therapeutic uses of the methods and compositions, including autologous transplantation of treated cells into humans for treatment of Parkinson's and other neuronal disorders.

Full Title Citati	on Front Review	Classification Dat	e Reference	Sequences	Attachments	Claims	KMMC	Draw Desi

# ☐ 42. Document ID: US 20030109041 A1

L26: Entry 42 of 189 File: PGPB Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109041

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109041 A1

TITLE: Lineage restricted glial precursors from the central nervous system

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Rao, Mahendra S. Salt Lake City UT US
Noble, Mark Brighton NY US

Mayer-Proschel, Margot Pittsford NY US

US-CL-CURRENT: 435/368

# ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

☐ 43. Document ID: US 20030109039 A1

L26: Entry 43 of 189

File: PGPB

Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109039

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109039 A1

TITLE: Enriched central nervous system stem cell and porgenitor cell populations, and

methods for identifying, isolating and enriching for such populations

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

Weissman, Irving

NAME CITY STATE COUNTRY RULE-47

Buck, David W. Uchida, Nobuko

Heathfield CA GB Palo Alto CAUS Redwood City US

US-CL-CURRENT: 435/368; 435/7.21

ABSTRACT:

Enriched neural stem and progenitor cell populations, and methods for identifying, isolating and enriching for neural stem cells using reagent that bind to cell surface markers, are provided.

Full   Title   Citation   Front   Review   Classification   Date   Reference   Sequ	mana di 1944 a di manda di 1951 di 1952 di 1951 di 195
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☐ 44. Document ID: US 20030109008 A1

L26: Entry 44 of 189 File: PGPB Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030109008

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030109008 A1

TITLE: Methods of making CDNA libraries

PUBLICATION-DATE: June 12, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Weiss, Samuel Alberta RΙ CA Reynolds, Brent Alberta CA RT Hammang, Joseph P. Barrington US Baetge, E. Edward Barrington US

US-CL-CURRENT: 435/91.1; 435/368

ABSTRACT:

The invention discloses methods of proliferation and differentiation of multipotent neural stem cells. Also provided are methods of making cDNA libraries and methods of screening biological agents which affect proliferation differentiation survival phenotype or function of CNS cells.

Full Title Citation Front Review Classification Date F	eference Sequences /	Attachments Claims KMC Draw Desc
☐ 45. Document ID: US 20030104997 A1	,	
L26: Entry 45 of 189	File: PGPB	Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030104997

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030104997 A1

TITLE: Multi-lineage directed induction of bone marrow stromal cell differentiation

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Black, Ira B. Skillman NY US
Woodbury, Dale Piscataway NJ US

US-CL-CURRENT: 514/12; 435/372, 514/44

# ABSTRACT:

Methods of inducing differentiation of mammalian bone marrow stromal cells into cells of multiple embryonic lineages by contacting marrow stromal cells with precursor differentiation-inducing compounds followed by contacting the partially differentiated precursor cells with specific cell type differentiation-inducing compounds. In one embodiment, the MSC derived precursor cell cultures comprise cells, at least some of which simultaneously express markers that are characteristic of endodermal and ectodermal cell types. In another embodiment, the differentiated cells are insulin-secreting pancreatic islet cells. Precursor differentiation-inducing compounds of the invention include anti-oxidants such as, but not limited to, betamercaptoethanol, dimethylsulfoxide, butylated hydroxyanisole, butylated hydroxytoluene, ascorbic acid, dimethylfumarate, and n-acetylcysteine. Endodermal cell differentiation-inducing compounds of the invention include but are not limited to anti-oxidants and growth factors including basic fibroblast growth factor. Once induced to differentiate into a particular cell type, the cells can be used for cell therapy, gene therapy, or both, for treatment of diseases, disorders, or conditions associated with tissues of multiple embryonic origins.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments Claims	KMMC   Draw Desc
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☐ 46. Document ID: US 20030103949 A1			
L26: Entry 46 of 189	File: PGPB	J	un 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030103949

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030103949 A1

TITLE: Screening small molecule drugs using neural cells differentiated from human embryonic stem cells

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	
Denham, Jerrod J.	San Francisco	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Thies, R. Scott	Pleasanton	CA	US	

US-CL-CURRENT: 424/93.21; 435/368, 435/4

#### ABSTRACT:

This invention provides populations of neural progenitor cells and differentiated neurons, obtained by culturing pluripotent cells in special growth cocktails. The technology can be used to produce progenitors that proliferate through at least .about.40 doublings, while maintaining the ability to differentiate into a variety of different neural phenotypes, including dopaminergic neurons. The neural progenitors and terminally differentiated neurons of this invention can be generated in large quantities for use in drug screening and the treatment of neurological disorders.

Full	Title Citation	Front   Review	Classification	Date   Reference	Sequences	Attachments	Claims	KMMC	Draw, Desi
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	47. Docume	ent ID: US 2	0030095956	5 A1					
L26: F	Entry 47 of	189		File:	PGPB		Мау	22,	2003

PGPUB-DOCUMENT-NUMBER: 20030095956

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030095956 A1

TITLE: Methods of proliferating undifferentiated neural cells

PUBLICATION-DATE: May 22, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Weiss, Samuel	Alberta	RI	CA	
Reynolds, Brent	Alberta	RI	CA	
Hammang, Joseph P.	Barrington		US	
Baetge, E. Edward	Barrington		US	

US-CL-CURRENT: 424/93.21; 435/368

# ABSTRACT:

The invention discloses methods of proliferation and differentiation of multipotent neural stem cells. Also provided are methods of making cDNA libraries and methods of screening biological agents which affect proliferation differentiation survival phenotype or function of CNS cells.

# ☐ 48. Document ID: US 20030092176 A1

L26: Entry 48 of 189

File: PGPB

May 15, 2003

PGPUB-DOCUMENT-NUMBER: 20030092176

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030092176 A1

TITLE: Ependymal neural stem cells and method for their isolation

PUBLICATION-DATE: May 15, 2003

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Janson, Ann Marie	Stockholm	MA	SE	
Frisen, Jonas	Stockholm		SE	
Johansson, Clas	Stockholm		SE	
Momma, Stefan	Spinga		SE	
Clarke, Diana	Cambridge		US	
Zhao, Ming	Solna		SE	
Lendahl, Urban	Stockholm		SE	
Delfani, Kioumars	Solna		SE	

US-CL-CURRENT: 435/368

# ABSTRACT:

The invention relates to an ependymal neural CNS stem cell, which cell expresses the surface protein Notch 1 together with at least one surface protein chosen from the group of Notch 2, Notch 3, CAR (transmembrane protein binding adenovirus) and CFTR cystic fibrosis transmembrane conductance regulator), and which cell also comprises at least one cilium. The invention also relates to preparations, including pharmaceutical preparations, comprising ependymal neural CNS stem cells, in vitro and in vivo assays based thereon and various other uses of the novel ependymal cells according to the invention.

Full	Title Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Drawi Desi

# ☐ 49. Document ID: US 20030082802 A1

L26: Entry 49 of 189

File: PGPB

May 1, 2003

PGPUB-DOCUMENT-NUMBER: 20030082802

PGPUB-FILING-TYPE: original-publication-amended

DOCUMENT-IDENTIFIER: US 20030082802 A1

TITLE: METHOD FOR NEURAL STEM CELL DIFFERENTIATION USING 5HT1A AGONISTS

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Rajan , Prithi

Rockville

Maryland

US

Altar , C. Anthony

Garrett Park

Maryland

US

US-CL-CURRENT: 435/368; 514/1

### ABSTRACT:

The present invention relates to a method for differentiating a neural stem cell into a neuronal cell such as a neuroblast or a neuron in vitro or in vivo. Particularly, the invention provides for a method for neural stem cell differentiation by contacting the neural stem cell with a 5HT1A ligand or agonist.

Full	Title Citation F	ront Review	Classification D	ate   Reference   :	Sequences	Attachments	Claims	KWIC	Draw, Desi
								***************************************	
	50. Documen	nt ID: US 20	0030082515 /	41					
1,26:	Entry 50 of 1	189		File:	PGPB		Ma	v 1.	2003

PGPUB-DOCUMENT-NUMBER: 20030082515

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030082515 A1

TITLE: Methods of screening biological agents

PUBLICATION-DATE: May 1, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Weiss, Samuel	Alberta	RI	CA	
Reynolds, Brent	Alberta	RI	CA	
Hammang, Joseph P.	Barrington		US	•
Baetge, E. Edward	Barrington		US	

US-CL-CURRENT: 435/4; 435/368

# ABSTRACT:

The invention discloses methods of proliferation and differentiation of multipotent neural stem cells. Also provided are methods of making cDNA libraries and methods of screening biological agents which affect proliferation differentiation survival phenotype or function of CNS cells.

Full Title Citation Front Review Classification Date R	eference Sequence	s Attachments	Claims KWC Draw Desc
☐ 51. Document ID: US 20030082160 A1			
L26: Entry 51 of 189	File: PGPB		May 1, 2003

PGPUB-DOCUMENT-NUMBER: 20030082160

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030082160 A1

TITLE: Differentiation of whole bone marrow

PUBLICATION-DATE: May 1, 2003

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yu, John S.	Los Angeles	CA	US	
Kabos, Peter	Los Angeles	CA	US	
Ehtesham, Moneeb	Los Angeles	CA	US	

US-CL-CURRENT: 424/93.21; 435/368

### ABSTRACT:

A method is described for generating a clinically significant volume of neural progenitor cells from whole bone marrow. A mass of bone marrow cells may be grown in a culture supplemented with fibroblast growth factor-2 ( $\underline{FGF-2}$ ) and epidermal growth factor ( $\underline{EGF}$ ). Further methods of the present invention are directed to utilizing the neural progenitor cells cultured in this fashion in the treatment of various neuropathological conditions, and in targeting delivery of cells transfected with a particular gene to diseased or damaged tissue.

Full	Title Citation Front f	Review   Classification	Date   Reference   S	Sequences	Attachments Claim	s KWMC Draw Desc
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	52. Document ID:	US 20030082152	A1			
L26:	Entry 52 of 189		File:	PGPB		May 1, 2003

PGPUB-DOCUMENT-NUMBER: 20030082152

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030082152 A1

TITLE: Adipose-derived stem cells and lattices

PUBLICATION-DATE: May 1, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hedrick, Marc H.	Encino	CA	US	
Katz, Adam J.	Charlottesville	VA	US	
Llull, Ramon	Mallorca	PA	ES	
Futrell, J. William	Pittsburgh	CA	US	
Benhaim, Prosper	Encino	CA	US	
Lorenz, Hermann Peter	Belmont	CA	US	
Zhu, Min	Los Angeles		US.	

US-CL-CURRENT: 424/93.21; 435/366

### ABSTRACT:

The present invention provides adipose-derived stem cells (ADSCs), adipose-derived stem cell-enriched fractions (ADSC-EF) and adipose-derivedlattices, alone and

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

combined with the ADSCs of the invention. In one aspect, the present invention provides an ADSC substantially free of adipocytes and red blood cells and clonal populations of connective tissue stem cells. The ADSCs can be employed, alone or within biologically-compatible compositions, to generate differentiated tissues and structures, both in vivo and in vitro. Additionally, the ADSCs can be expanded and cultured to produce molecules such as hormones, and to provide conditioned culture media for supporting the growth and expansion of other cell populations. In another aspect, the present invention provides a adipose-derived lattice substantially devoid of cells, which includes extracellular matrix material from adipose tissue. The lattice can be used as a substrate to facilitate the growth and differentiation of cells, whether in vivo or in vitro, into anlagen or even mature tissues or structures.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Drawn Desc
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	53.	Docum	ent ID	: US 2	003005993	9 A1						
L26:	Entr	y 53 of	189				File:	PGPB		Mar	27,	2003

PGPUB-DOCUMENT-NUMBER: 20030059939

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030059939 A1

TITLE: Trans-differentiation and re-differentiation of somatic cells and production

of cells for cell therapies

PUBLICATION-DATE: March 27, 2003

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Page, Raymond	Southbridge	MA	US	
Dominko, Tanja	Southbridge	MA	US	
Malcuit, Christopher	Hudson	MA	US	

US-CL-CURRENT: 435/366; 435/368, 435/372

# ABSTRACT:

The invention provides a method for effecting the trans-differentiation of a somatic cell, i.e., the conversion of a somatic cell of one cell type into a somatic cell of a different cell type. The method is practiced by culturing a somatic cell in the presence of at least one agent selected from the group consisting of (a) cytoskeletal inhibitors and (b) inhibitors of acetylation, and (c) inhibitors of methylation, and also culturing the cell in the presence of agents or conditions that induce differentiation to a different cell type. The method is useful for producing histocompatible cells for cell therapy.

Full Title Citation Front Review Classificat	rtion Date Reference Sequences Attac	chments Claims KMC Draw Des
☐ 54. Document ID: US 20030054	4973 A1	
L26: Entry 54 of 189	File: PGPB	Mar 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030054973

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030054973 A1

TITLE: Methods and compositions for the repair and/or regeneration of damaged

myocardium

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME CITY

STATE COUNTRY

RULE-47

Anversa, Piero

New York

NY

US

US-CL-CURRENT: 514/1; 435/372

### ABSTRACT:

Methods, compositions, and kits for repairing damaged myocardium and/or myocardial cells including the administration cytokines are disclosed and claimed.

Full	Title Citatio	n Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC	Draw Desi
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	55. Docu	ment ID:	US 2	003004983′	7 <b>A</b> 1						
L26:	Entry 55	of 189				File:	PGPB		Mar	13,	2003

PGPUB-DOCUMENT-NUMBER: 20030049837

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030049837 A1

TITLE: In vitro and in vivo proliferation and use of multipotent neural stem cells

and their progeny

PUBLICATION-DATE: March 13, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY RULE-47
Weiss, Samuel	Alberta	RI	CA
Reynolds, Brent	Alberta	RI	CA
Hammang, Joseph P.	Barrington		US
Baetge, E. Edward	Barrington		US

US-CL-CURRENT: 435/368; 435/384

# ABSTRACT:

Nucleic acids may be obtained from neural cell cultures produced by using growth factors to induce the proliferation of multipotent neural stem cells. The resultant progeny may be passaged repeatedly to produce a sufficient number of cells to obtain representative nucleic acid samples. Clonal cultures may be produced. Nucleic acids may be obtained from both cultured normal and dysfunctional neural cells and from neural cell cultures at various stages of development. This information allows for the identification of the sequence of gene expression during neural development and can be used to reveal the effects of biological agents on gene expression in neural cells. Additionally, nucleic acids derived from dysfunctional tissue can be compared with that of normal tissue to identify genetic material which may be the cause of the

dysfunction. This information could then be used in the design of therapies to treat the neurological disorder. A further use of the technology would be in the diagnosis of genetic disorders or for use in identifying neural cells at a particular stage in development.

Full Title Citation Front Review Classification Date Reference Sequ	uences Attachments Claims KWC Draw Des
☐ 56. Document ID: US 20030044389 A1	

File: PGPB

Mar 6, 2003

PGPUB-DOCUMENT-NUMBER: 20030044389

PGPUB-FILING-TYPE: new

L26: Entry 56 of 189

DOCUMENT-IDENTIFIER: US 20030044389 A1

TITLE: Microarrays for cell phenotyping and manipulation

PUBLICATION-DATE: March 6, 2003

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Brown, Patrick O.	Stanford	CA	US	
Soen, Yoav	Palo Alto	CA	US	•
Keen, Erica	Melrose Park	PA	បន	

US-CL-CURRENT: 424/93.7; 435/7.21

# ABSTRACT:

Cells are profiled with respect to their expression of cell surface molecules, and ability to respond to external stimulus in the microenvironment. External stimuli include cell-cell interactions, response to factors, and the like. The cells are arrayed on a planar or three-dimensional substrate through binding to immobilized or partially diffused probes. Probes of interest include specific binding partners for cell surface molecules, signaling cues that act to regulate cell responses, differentiation factors, etc., which may be arrayed as one or a combination of molecules.

Ĩ	Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw, Desi
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		57.	Docum	ent ID	): US 2	003004011	1 A1			,			
]	L26:	Entr	y 57 of	189				File:	PGPB		Feb	27,	2003

PGPUB-DOCUMENT-NUMBER: 20030040111

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030040111 A1

TITLE: Differentiated cells suitable for human therapy

PUBLICATION-DATE: February 27, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Gold, Joseph D.

San Francisco

CA US

Lebkowski, Jane S.

Portola Valley

CA

US

US-CL-CURRENT: <u>435</u>/<u>368</u>; <u>435</u>/<u>366</u>, <u>435</u>/<u>370</u>

### ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

Full	Title	Citation Fr	ont Review				Sequences	Attachments	Claims	KWIC	Draw, Desi
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L26:	Entr	y 58 of 1	.89			File:	PGPB		Feb	20,	2003

PGPUB-DOCUMENT-NUMBER: 20030036509

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030036509 A1

TITLE: TGF-alpha polypeptides, functional fragments and methods of use therefor

PUBLICATION-DATE: February 20, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Twardzik, Daniel R.	Bainbridge Island	WA	US	
Pernet, Andre	Lake Forest	IL	US	
Felker, Thomas S.	Vashon	WA	US	
Paskell, Stefan	Bainbridge Island	WA	US ·	
Reno, John M.	Brier	WA	US	

US-CL-CURRENT: 514/12; 530/399

### ABSTRACT:

Disclosed are TGF-60 mimetics that PEGylated TGF-.alpha. polypeptides and PEGylated TGF-60 related polypetides or fragments thereof.

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26.0	11111	Citation	FIGURE	U sinteat	Glassingation	Date	Mererance	Ochici i ces	Attachments	Cialitis	Model	D1300 D451

# ☐ 59. Document ID: US 20030032187 A1

L26: Entry 59 of 189 File: PGPB Feb 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030032187

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030032187 A1

TITLE: Selective antibody targeting of undifferentiated stem cells

PUBLICATION-DATE: February 13, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

McWhir, Jim Midlothian CA GB Gold, Joseph D. San Francisco CA US

Schiff, J. Michael Menlo Park US

US-CL-CURRENT: 435/455; 435/366

### ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in expression of a cell-surface antigen that can be used to deplete the undifferentiated cells. Model effector sequences encode glycosyl transferases that synthesize carbohydrate xenoantigen or alloantigen, which can be used for immunoseparation or as a target for complement-mediated lysis. The differentiated cell populations produced are suitable for use in tissue regeneration and non-therapeutic applications such as drug screening.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw. Desc
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☐ 60. Document ID: US 20030032181 A1

L26: Entry 60 of 189 File: PGPB Feb 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030032181

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030032181 A1

TITLE: Production of radial glial cells

PUBLICATION-DATE: February 13, 2003

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Weiss, Samuel Calgary CA Gregg, Christopher Calgary CA

US-CL-CURRENT: 435/368

ABSTRACT:

The present invention relates to a method of producing radial glial cells from neural stem cells, particularly by contacting neural stem cells with epidermal growth factor (EGF), fibroblast growth factor 2 ( $\underline{FGF-2}$ ) and/or TGF.alpha. Leukemia inhibitory factor (LIF) and ciliary neurotrophic factor (CNTF) can optionally be added to enhance the effect of EGF,  $\underline{FGF-1}$  or TGF.alpha. Also provided are methods of producing radial glial cells from ependymal cells, as well as methods of proliferating ependymal cells.

Full	Title Citatio	n Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Drawi Desi
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	61. Docu	ment ID	: US 2	0030031651	l Al						
L26:	Entry 61	of 189				File:	PGPB		Feb	13,	2003

PGPUB-DOCUMENT-NUMBER: 20030031651

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030031651 A1

TITLE: Methods and reagents for cell transplantation

PUBLICATION-DATE: February 13, 2003

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lee, Ike W.	Norwood	MA	US	
Liu, Guizhen	Norwood	MA	US	
Hampe, James	Dedham	MA	US	
Croissant, Jeffrey D.	Scituate	MA	US	

US-CL-CURRENT: 424/93.7; 435/366

# ABSTRACT:

The invention features methods for producing cells for transplantation into myocardial tissue of a mammal (e.g., a human). The method includes the steps of (a) providing a population of bone marrow stem cells; (b) culturing the cells under conditions that induce the cells to become cardiomyogenic cells; (c) monitoring the state of differentiation of the cells of step (b); and (d) collecting the cells of step (b) when at least about 10% and as many as 100% of the cells are cardiomyogenic cells. The bone marrow stem cells can be, for example, human bone marrow stem cells. In one embodiment, the method includes the step of transplanting the differentiated stem cells into a mammal (e.g., a human).

Full	Title Citation	Front Review	Classification Da	te Reference	Sequences	Attachments	Claims	KMC	Draw, Desc
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<b>-</b>	(A )	. TD . 110 0	00000000001						
Ц	62. Docum	ient ID: US 2	0030027331 A	<b>X1</b>					
L26:	Entry 62 of	£ 189		File	: PGPB		Fe	b 6,	2003

PGPUB-DOCUMENT-NUMBER: 20030027331

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030027331 A1

TITLE: Isolated homozygous stem cells, differentiated cells derived therefrom, and http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

materials and methods for making and using same

PUBLICATION-DATE: February 6, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yan, Wen Liang	Potomac	MD	US	
Huang, Steve Chien-Wen	Germantown	MD	US	
Nguyen, Minh-Thanh	Rockville	MD	US	
Lin, Hua	N. Potomac	MD	US	
Jingqi, Lei	Gaithersburg	MD	US	
Khanna, Ruchi	Germantown	MD	US	

US-CL-CURRENT: 435/366

#### ABSTRACT:

The present invention discloses and describes pluripotent homozygous stem (HS) cells, and methods and materials for making same. The present invention also provides methods for differentiation of HS cells into progenitor (multipotent) cells or other desired cells, groups of cells or tissues. Further, the applications of the HS cells disclosed herein, include (but are not limited to) the diagnosis and treatment of various diseases (for example, genetic diseases, neurodegenerative diseases, endocrine-related disorders and cancer), traumatic injuries, cosmetic or therapeutic transplantation, gene therapy and cell replacement therapy.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KiMC	Draw Desc
			,									
	63.	Docum	ent II	): US 2	003001751	0 <b>A</b> 1			······	***************************************	••••	***************************************

File: PGPB

PGPUB-DOCUMENT-NUMBER: 20030017510

PGPUB-FILING-TYPE: new

L26: Entry 63 of 189

DOCUMENT-IDENTIFIER: US 20030017510 A1

TITLE: Encapsulated cell indicator system

PUBLICATION-DATE: January 23, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lee, Ike W.	Norwood	MA	US	
Ballica, Rabia	Framingham	MA	US	
Croissant, Jeffrey D.	Scituate	MA	US	

US-CL-CURRENT: 435/7.21

# ABSTRACT:

The invention features an encapsulated cell indicator system that includes (a) indicator cells having a signal-responsive element operably linked to a reporter gene; (b) encapsulating material; and (c) a permeable membrane. In this encapsulated cell indicator system, the indicator cells are encapsulated in the encapsulated

Jan 23, 2003

material and the encapsulated material and the indicator cells are surrounded by the permeable membrane.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Desc ☐ 64. Document ID: US 20030013193 A1

L26: Entry 64 of 189

File: PGPB

Jan 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030013193

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030013193 A1

TITLE: Method of producing region-specific neurons from human neuronal stem cells

PUBLICATION-DATE: January 16, 2003

INVENTOR-INFORMATION:

NAME

STATE

COUNTRY

RULE-47

Wu, Ping

League City

TX

US-CL-CURRENT: 435/368

### ABSTRACT:

A method of priming neural stem cells in vitro by adhesively culturing in a mixture of basic fibroblast growth factor, laminin and heparin to differentiate into specific neuronal phenotypes, including cholinergic, glutamatergic and GABAergic neurons, in a region-specific manner, when transplanted in vivo.

Full   Title   Citation   Front   Review   Classification   Date	Reference   S	Sequences	Attachments	Claims	киис	Draw, Desc
☐ 65. Document ID: US 20030013192 A1						
L26: Entry 65 of 189	File:	PGPB	•	Jan	16,	2003

PGPUB-DOCUMENT-NUMBER: 20030013192

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030013192 A1

TITLE: Method for neural stem cell differentiation using valproate

Falls Church

PUBLICATION-DATE: January 16, 2003

INVENTOR-INFORMATION:

Pitts, Lee

RULE-47 COUNTRY STATE CITY NAME US DC Washington Laeng, Pascal Gaithersburg US MDMallon, Barbara

US-CL-CURRENT: 435/368; 514/557

VΑ

### ABSTRACT:

The present invention relates to a method for differentiating a neural stem cell into a neuronal cell such as a neuroblast or neuron in vitro or in vivo. Particularly, the invention provides for a method for neural stem cell differentiation by contacting the neural stem cell with a valproate compound or analog thereof.

Full Title	Citation Front	Review Classification	Date Reference	Sequences Atta	chments Claims	KMIC   Draw Desc
П ((	Danis and ID	. TIC 20020002 <i>57</i>	4 4 1			

☐ 66. Document ID: US 20030003574 A1

L26: Entry 66 of 189

File: PGPB

Jan 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030003574

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030003574 A1

TITLE: Multipotent stem cells from peripheral tissues and uses thereof

PUBLICATION-DATE: January 2, 2003

### INVENTOR-INFORMATION:

MAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Montreal		CA	
Akhavan, Mahnaz	Montreal		CA	
Fernandes, Karl J. L.	Montreal		CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Montreal		CA	

US-CL-CURRENT: 435/368

# ABSTRACT:

This invention relates to multipotent stem cells, purified from the peripheral tissue of mammals, and capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Full Title Citation Front Review Classification Date	Reference Sequences	Attachments 0	Claims KWWC	Draw, Desi
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☐ 67. Document ID: US 20030003478 A1				
L26: Entry 67 of 189	File: PGPB	*	Jan 2,	2003

PGPUB-DOCUMENT-NUMBER: 20030003478

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030003478 A1

TITLE: Identifying and characterizing genes

PUBLICATION-DATE: January 2, 2003

INVENTOR-INFORMATION:

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

NAME

CITY

STATE

COUNTRY

RULE-47

Depinho, Ronald A.

Brookline

US

Chin, Lynda

Brookline

MA ΜA

US

US-CL-CURRENT: 435/6; 435/455

### ABSTRACT:

The invention provides methods and materials for identifying and characterizing genes related to phenotypes such as cancer and cell survivability. Also provided in the invention are cells and transgenic, non-human mammals that can be used in these methods.

Full Title Citation	Front Review Classification	on Date Reference Sei	quences Attachments Claims	KMC Draw, Des
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			·	
<b>—</b>	TD TTG			

☐ 68. Document ID: US 20020193301 A1

L26: Entry 68 of 189

File: PGPB

Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020193301

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020193301 A1

TITLE: TGF-alpha polypeptides, functional fragments and methods of use therefor

PUBLICATION-DATE: December 19, 2002

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Twardzik, Daniel R.	Bainbridge Island	WA	US	
Pernet, Andre	Lake Forest	IL	US	
Felker, Thomas S.	Vashon	WA	US	
Paskell, Stefan	Bainbridge Island	WA	US	

US-CL-CURRENT: 514/12

# ABSTRACT:

Disclosed are TGF-.alpha. polypeptides, related polypeptides, fragments and mimetics thereof useful in stimulating cell or precursor cell proliferation, migration and differentiation. The methods of the invention are useful to treat tissue injury as well as expand stem cell populations in, or obtained from, gastrointestinal, musculoskeletal, urogenital, neurological and cardiovascular tissues. The methods include ex vivo and in vivo applications.

Full Title Citation Front Review CI	assification Date Reference	Sequences Attachments	Claims KMC Draw Desi
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☐ 69. Document ID: US 200	20169119 A1		
L26: Entry 69 of 189	File	PGPB	Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020169119

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020169119 A1

TITLE: TGF-alpha polypeptides, functional fragments and methods of use therefor

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

STATE RULE-47 NAME CITY COUNTRY WA Twardzik, Daniel R. Bainbridge Island US Pernet, Andre Lake Forest ILUS Felker, Thomas S. Vashon WA US Paskell, Stefan Bainbridge Island WA US

US-CL-CURRENT: 514/12

# ABSTRACT:

Disclosed are TGF-.alpha. polypeptides, related polypeptides, fragments and mimetics thereof useful in stimulating stem cell or precursor cell proliferation, migration and differentiation. The methods of the invention are useful to treat tissue injury as well as expand stem cell populations in, or obtained from, gastrointestinal, musculoskeletal, urogenital, neurological and cardiovascular tissues. The methods include ex vivo and in vivo applications.

Full	Titl∈	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw, Desi
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☐ 70. Document ID: US 20020168767 A1

L26: Entry 70 of 189 File: PGPB Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168767

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168767 A1

TITLE: Method of isolating human neuroepithelial precursor cells from human fetal

tissue

PUBLICATION-DATE: November 14, 2002

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Mayer-Proschel, Margot	Pittsford	NY	US	
Rao, Mahendra S.	Salt Lake City	UT	US	
Tresco, Patrick A.	Sandy	UT	US	
Messina, Darin J.	Salt Lake City	UT	US	

US-CL-CURRENT: 435/368; 800/8

# ABSTRACT:

A method for isolating human neuroepithelial precursor cells from human fetal tissue by culturing the human fetal cells in fibroblast growth factor and chick embryo extract and immunodepleting from the cultured human fetal cells any cells expressing

A2B5, NG2 and eNCAM is provided. In addition, methods for transplanting these cells into an animal are provided. Animals models transplanted with these human neuroepithelial precursor cells and methods for monitoring survival, proliferation, differentiation and migration of the cells in the animal model via detection of human specific markers are also provided.

Full	Title	Citation	Front	Review	Classificat	tion C	) ate	Reference	Sequences	Attachme	ents (	laims	KMIC	Drawl Desi
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	71	Danima	ant III.	TICO	0020169	2766	A 1							
L	/1.	Docume	ant ID.	US 2	.0020100	5/00	ΑI							
L26:	Entry	y 71 of	189					File:	PGPB			Nov	14,	2002
	71.	Docume	ent ID:							ennement en				

PGPUB-DOCUMENT-NUMBER: 20020168766

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168766 A1

TITLE: Genetically altered human pluripotent stem cells

PUBLICATION-DATE: November 14, 2002

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Gold, Joseph D.	San Francisco	CA	US	
Carpenter, Melissa K.	Castro Valley	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Xu, Chunhui	Cupertino	CA	US	

US-CL-CURRENT: 435/366; 435/455

# ABSTRACT:

This disclosure provides a system for obtaining genetically altered primate pluripotent stem (pPS) cells. The pPS cells are maintained in an undifferentiated state by culturing on a feeder cell line that has been immortalized and altered with drug resistance genes. Alternatively, the role of the feeder cells is replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. The cells can be genetically altered with a viral vector or DNA/lipid complex, and then selected for successful transfection by drug-resistant phenotype in the transfected cells. The system allows for bulk proliferation of genetically altered pPS cells as important products for use in human therapy or drug screening.

Full	Title Citati	on Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desi
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	72. Doc	ument ID	: US 2	002016876	3 A1						
L26:	Entry 72	of 189				File:	PGPB		Nov	14,	2002

PGPUB-DOCUMENT-NUMBER: 20020168763

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168763 A1

TITLE: Isolated homozygous stem cells, differentiated cells derived therefrom, and materials and methods for making and using same

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

PUBLICATION-DATE: November 14, 2002

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yan, Wen Liang	Potomac	MD	US	
Huang, Steve Chien-Wen	Germantown	MD.	US	
Nguyen, Minh-Thanh	Rockville	MD	US	
Lin, Hua (Helen)	Potomac	MD	US	
Lei, Jingqi	Gaithersburg	MD	US	
Khanna, Ruchi	Germantown	MD	US	

US-CL-CURRENT: 435/325; 435/350, 435/354, 435/366

### ABSTRACT:

The present invention discloses and describes pluripotent homozygous stem (HS) cells, and methods and materials for making same. The present invention also provides methods for differentiation of HS cells into progenitor (multipotent) cells or other desired cells, groups of cells or tissues. Further, the applications of the HS cells disclosed herein, include (but are not limited to) the diagnosis and treatment of various diseases (for example, genetic diseases, neurodegenerative diseases, endocrine-related disorders and cancer), traumatic injuries, cosmetic or therapeutic transplantation, gene therapy and cell replacement therapy.

Full Title	Citation Front Review Classification Date Reference Sequences Attachments Claims KWIC Draw Des
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$\square$ 73.	Document ID: US 20020168350 A1

L26: Entry 73 of 189

File: PGPB

Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020168350

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168350 A1

TITLE: Methods for treating disorders of neuronal deficiency with bone marrow-derived

cells

PUBLICATION-DATE: November 14, 2002

INVENTOR-INFORMATION:

RULE-47 COUNTRY NAME CITY STATE

Brazelton, Timothy R. Cupertino CA US Menlo Park CA US Blau, Helen M.

US-CL-CURRENT: 424/93.21; 424/93.7

### ABSTRACT:

The invention provides novel methods of treating neurological disorders which result in the loss of neurons (neuronal deficiencies). Bone marrow-derived cells are administered to individuals suffering from neuronal deficiencies. Administration of bone marrow-derived cells results in formation of new neurons in the nervous system, thereby replacing lost neurons. The methods of the invention may also be used for memory augmentation in memory impaired individuals.

☐ 74. Document ID: US 20020164794 A1

L26: Entry 74 of 189

File: PGPB

Nov 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020164794

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164794 A1

TITLE: Human cord blood derived unrestricted somatic stem cells (USSC)

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Wernet, Peter

Duesseldorf

US-CL-CURRENT: <u>435/372</u>

ABSTRACT:

A composition in human cord and placental blood which comprises unrestricted somatic stem cells is described here which can be amplified in vitro to large quantities sufficient for medical applications as regenerative medicines. Initiation and maintenance as well as ex vivo expansion protocols of such stem cells from cord blood is described.

Furthermore, it is shown that from these cells employing varying differentiation induction protocols distinct lineage progenitors for hematopoiesis and endothel, as well as mesenchymal progenitors for muscle bone, cartilage and fat as well as neural progenitors can be cultured and expanded for use in regenerative medicine.

Full Title Citation Front	Classification	Data Batarana	Campanese	Attachments	Claima	KWIC Draw, Desi
run   nue   Citation   Fight	Mediano   Classification	hare i weletative	Sednemes	Attachments	Piglitte	. Koolo   D1300 De30
	i					

☐ 75. Document ID: US 20020164791 A1

L26: Entry 75 of 189

File: PGPB

Nov 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020164791

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164791 A1

TITLE: Primitive neural stem cells and method for differentiation of stem cells to

neural cells

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Van Der Kooy, Derek Toronto MA CA HS

Tropepe, Vincent Boston US-CL-CURRENT: 435/366

### ABSTRACT:

Described are a novel cell type in the neural lineage, and method of producing the same based on the degree of neural commitment and growth factor responsiveness in vitro and the potential to give rise to neural and non-neural progeny in vivo. The novel veil type of neural lineage and cells derived therefrom have a number of applications including applications regarding tissue engineering, transplantation and gene therapy and drug discovery. Also described are suggested uses of the method and cell type including isolating genes that positively and negatively regulate the transmission from an ES cell to a neural cell and generally for studying ES cell models of mammalian neural development.

Full Title Citation Front Review Classificatio	on   Date   Reference   Sequences   Attach	ments Claims KMC Draw. Desi
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T 76 D ID 110 000001646	200 41	•
☐ 76. Document ID: US 200201643	309 A I	
L26: Entry 76 of 189	File: PGPB	Nov 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020164309

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164309 A1

TITLE: Cultures of human CNS neural stem cells

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Carpenter, Melissa Foster City CA US

US-CL-CURRENT: 424/93.7; 435/368

### ABSTRACT:

The invention provides a method for determining the effect of a biological agent comprising contacting a cell culture with a biological agent. The cell culture of the invention contains a culture medium containing one or more preselected growth factors effective for inducing multipotent central nervous system (CNS) neural stem cell proliferation. The cell culture also contains, suspended in the culture medium, human multipotent CNS neural stem cells that are derived from primary CNS neural tissue that have a doubling rate faster than 30 days.

Full Title Citation Front Review Classification Date	Reference :	Sequences	Attachments	Claims	KWC	Drawi Desi
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☐ 77. Document ID: US 20020164308 A1						
L26: Entry 77 of 189	File:	PGPB		No	v 7,	2002

PGPUB-DOCUMENT-NUMBER: 20020164308

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164308 A1

TITLE: Embryonic stem cells and neural progenitor cells derived therefrom

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Reubinoff, Benjamin Eithan Mevaseret Zign IL
Pera, Martin Frederick Prshrab Victoria AU
Ben-Hur, Tamir Jerusalem IL

US-CL-CURRENT: 424/93.7; 435/366, 435/368

### ABSTRACT:

The present invention relates to undifferentiated human embryonic stem cells, methods of cultivation and propagation and production of differentiated cells. In particular it relates to the production of human ES cells capable of yielding somatic differentiated cells in vitro, as well as committed progenitor cells such as neural progenitor cells capable of giving rise to mature somatic cells including neural cells and/or glial cells and uses thereof.

This invention provides methods that generate in vitro and in vivo models of controlled differentiation of ES cells towards the neural lineage. The model, and cells that are generated along the pathway of neural differentiation may be used for: the study of the cellular and molecular biology of human neural development, discovery of genes, growth factors, and differentiation factors that play a role in neural differentiation and regeneration, drug discovery and the development of screening assays for teratogenic, toxic and neuroprotective effects.

Full	· · · · · · · · · · · · · · · · · · ·	Review Classification	<u> </u>	<u> </u>	 <del>'</del>	
		D: US 20020155440				•
L26:	Entry 78 of 189	)	File	: PGPB	Oct 2	24, 2002

PGPUB-DOCUMENT-NUMBER: 20020155440

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020155440 A1

TITLE: Using overexpression of laminin alpha 4 subunit as a diagnostic and prognostic

indicator of malignant tumors

PUBLICATION-DATE: October 24, 2002

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ljubimova, Julia Y.	Studio City	CA	US	
Ljubimov, Alexander V.	Studio City	CA	US	
Black, Keith L.	Los Angeles	CA	US	

US-CL-CURRENT: 435/6; 435/7.23

# ABSTRACT:

Disclosed is a method of diagnosing the presence of a malignant tumor, including a http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

glioma, in a human subject, which involves detecting overexpression of laminin .alpha.4 subunit protein or laminin .alpha.4-specific MRNA, compared to the expression level in a normal tissue control. Also disclosed are a method of predicting the recurrence of a malignant tumor in a human subject from whom a malignant tumor has been resected and a method of classifying the grade of a malignant tumor, such as a glial tumor, based on a molecular classification.

Full Title Citation Front Review Classific	ation Date Reference Sequences Att	achments   Claims   KMC   Draw Desi
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☐ 79. Document ID: US 2002015	51056 A1	
L26: Entry 79 of 189	File: PGPB	Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020151056

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020151056 A1

TITLE: Novel differentiation inducing process of embryonic stem cell to ectodermal

cell and its use

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Sasai, Yoshiki Kyoto JP
Nishikawa, Shin-Ichi Kyoto JP

US-CL-CURRENT: 435/368

# ABSTRACT:

A method for inducing differentiation of an embryonic stem cell into an ectodermal cell and an ectoderm-derived cell, which comprises culturing the embryonic stem cell under non-aggregation conditions; a medium and a medium supernatant used in the method; an agent for inducing differentiation used in the method; a stroma cell or a stroma cell-derived factor having activity of inducing differentiation in the method; an antibody which specifically recognizes the stroma cell; an antigen which recognizes the antibody; a cell induced by the method; a method for evaluating or screening a substance relating to the regulation in a differentiation step from an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell by carrying out the method; and a medicament comprising the stroma cell, the stroma cell-derived cell, the antibody, the antigen or the cell.

	Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	K004C	Draw Desi
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		80.	Docume	ent ID:	US 2	002015105	3 A1						
L	26:	Entry	, 80 of	189				File:	PGPB		Oct	17,	2002

PGPUB-DOCUMENT-NUMBER: 20020151053

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020151053 A1

TITLE: Direct differentiation of human pluripotent stem cells and characterization of

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

differentiated cells

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Carpenter, Melissa K. Castro Valley CA US Funk, Walter D. Hayward CA US Thies, R. Scott Pleasanton CA US

US-CL-CURRENT: <u>435/366</u>

### ABSTRACT:

This invention provides a system for efficiently producing differentiated cells from pluripotent cells, such as human embryonic stem cells. Rather than permitting the cells to form embryoid bodies according to established techniques, differentiation is effected directly in monolayer culture on a suitable solid surface. The cells are either plated directly onto a differentiation-promoting surface, or grown initially on the solid surface in the absence of feeder cells and then exchanged into a medium that assists in the differentiation process. The solid surface and the culture medium can be chosen to direct differentiation down a particular pathway, generating a cell population that is remarkably uniform. The methodology is well adapted to bulk production of committed precursor and terminally differentiated cells for use in drug screening or regenerative medicine.

Full	Title Citation Front Review C	lassification   Date	Reference	Sequences	Attachments	Claims	KOMC	Draw, Desi
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	81. Document ID: US 200	)20146749 <b>A</b> 1						
L26:	Entry 81 of 189		File:	PGPB		Oct	10,	2002

PGPUB-DOCUMENT-NUMBER: 20020146749

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020146749 A1

TITLE: DIAGNOSIS AND TREATMENT OF NEUROECTODERMAL TUMORS

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

LYONS PH.D., SUSAN A. BIRMINGHAM AL US SONTHEIMER, HARALD W. BIRMINGHAM AL US

US-CL-CURRENT: 435/7.23; 435/7.1, 436/63, 436/64

# ABSTRACT:

The present invention provides fusion proteins for the detection and treatment of neuroectodermal tumors. Previous work demonstrated that chlorotoxin is specific for glial-derived or meningioma-derived tumor cells. The current invention has extended the use of chlorotoxin-cytotoxin fusion proteins to treat the whole class neuroectodermal tumors such as gliomas, meningiomas, ependymonas, medulloblastomas, neuroblastomas, gangliomas, pheochromocytomas, melanomas, PPNET's, small cell

carcinoma of the lung, Ewing's sarcoma, and metastatic tumors in the brain. Also, diagnostic methods are provided for screening neoplastic neuroectodermal tumors:

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Des-

□ 82. Document ID: US 20020142460 A1

L26: Entry 82 of 189

File: PGPB

Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142460

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020142460 A1

TITLE: Generation, characterization, and isolation of neuroepithelial stem cells and

lineage restricted intermediate precursor

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Salt Lake City Rao, Mahendra S. UT US

Mayer-Proschel, Margot Sandy UT US

US-CL-CURRENT: 435/368

### ABSTRACT:

Multipotent neuroepithelial stem cells and lineage-restricted oligodendrocyteastrocyte precursor cells are described. The neuroepithelial stem cells are capable of self-renewal and of differentiation into neurons, astrocytes, and oligodendrocytes. The oligodendrocyte-astrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into oligodendrocytes and astrocytes, but not neurons. Methods of generating, isolating, and culturing such neuroepithelial stem cells and oligodendrocyte-astrocyte precursor cells are also disclosed.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	Kelic	Draw Desi
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	83.	Docum	ent ID	: US 2	002013720	4 A 1						

L26: Entry 83 of 189 File: PGPB Sep 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020137204

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020137204 A1

TITLE: Techniques for growth and differentiation of human pluripotent stem cells

PUBLICATION-DATE: September 26, 2002

INVENTOR-INFORMATION:

NAME CTTY STATE COUNTRY RULE-47

Carpenter, Melissa K. Castro Valley CA

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.27&ref=26&dbname=PGPB,USPT,U... 10/27/04

Funk, Walter D. Hayward CA US Gold, Joseph D. San Francisco CA US Inokuma, Margaret S. San Jose CA US Xu, Chunhui Cupertino CA US

US-CL-CURRENT: 435/366

### ABSTRACT:

This disclosure provides an improved system for culturing human pluripotent stem (pPS) cells in the absence of feeder cells. The role of the feeder cells can be replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. Permanent cell lines are provided that can produce conditioned medium on a commercial scale. Methods have also been discovered to genetically alter pPS cells by introducing the cells with a viral vector or DNA/lipid complex. The system described in this disclosure allows for bulk proliferation of pPS cells for use in studying the biology of pPS cell differentiation, and the production of important products for use in human therapy.

Full	Title Citation Front Review Cla	ssification Date Reference	Sequences   Attachments	Claims   KMC   Draw Desc
	84. Document ID: US 2002	20127715 A1	······································	
L26:	Entry 84 of 189	File:	PGPB	Sep 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020127715

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020127715 A1

TITLE: Transfection of human embryonic stem cells

PUBLICATION-DATE: September 12, 2002

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Benvenisty, Nissim	Jerusalem		IL	
Yanuka, Ofra	Givat Zeev		IL	
Schuldiner, Maya	Moshav Aminadav		IL	
Eiges-Avner, Rachel	Mevasseret Zion		IL	

US-CL-CURRENT: 435/366; 435/455

### ABSTRACT:

Methods are provided for altering gene expression in a population of human embryonic cells that include introducing a gene expression altering sequence into cells the cells retaining their pluripotent character, for purifying pluripotent embryonic stem cells from a heterogeneous population of cells, and for treating a human suffering from a deficiency of a selected cell type. Reagent cell populations are further provided for supplying material for transplantation consisting essentially of pluripotent human embryonic stem cells modified by foreign genetic material.

# □ 85. Document ID: US 20020123465 A1

L26: Entry 85 of 189

File: PGPB

Sep 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020123465

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020123465 A1

TITLE: TGF-alpha polypeptides, functional fragments and methods of use therefor

PUBLICATION-DATE: September 5, 2002

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Twardzik, Daniel R.	Bainbridge Island	WA	US	
Pernet, Andre	Lake Forest	IL	US	
Felker, Thomas S.	Vashon	AW	US	
Paskell, Stefan	Bainbridge Island	WA	US	

US-CL-CURRENT: 514/12

### ABSTRACT:

Disclosed are TGF-.alpha. polypeptides, related polypeptides, fragments and mimetics thereof useful in stimulating stem cell or precursor cell proliferation, migration and differentiation. The methods of the invention are useful to treat tissue injury as well as expand stem cell populations in, or obtained from, gastrointestinal, musculoskeletal, urogenital, neurological and cardiovascular tissues. The methods include ex vivo and in vivo applications.

	ull	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw Desc
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☐ 86. Document ID: US 20020123143 A1

L26: Entry 86 of 189

File: PGPB

Sep 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020123143

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020123143 A1

TITLE: Multipotent stem cells from peripheral tissues and uses thereof

PUBLICATION-DATE: September 5, 2002

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Montreal		CA	
Akhavan, Mahnaz	Montreal		CA	
Fernandes, Karl J. L.	Montreal		CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Montreal		CA	

US-CL-CURRENT: 435/368

#### ABSTRACT:

This invention relates to multipotent stem cells, purified from the peripheral tissue of mammals, and capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Full Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Drawt Desc
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□ 87.	Document II	D: US 2	002011505	9 A1						
L26: Entry	7 87 of 189				File:	PGPB		Aug	22,	2002

PGPUB-DOCUMENT-NUMBER: 20020115059

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020115059 A1

TITLE: Drug screening system

PUBLICATION-DATE: August 22, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Terada, Naohiro Gainesville FL US
Hamazaki, Takashi Gainesville FL US

US-CL-CURRENT: 435/4; 435/354, 435/7.2, 435/7.21

# ABSTRACT:

A method for identifying a drug candidate for promoting tissue-specific differentiation of a stem cell includes the steps of: providing a library of test substances and an in vitro culture of stem cells divided into at least two subcultures; contacting one of the subcultures with the first test substance from the library and a second subculture with a second test substance from the library; culturing the subcultures under conditions that would promote tissue-specific differentiation of the stem cells if an agent that promoted tissue-specific differentiation was in contact with the stem cells; and analyzing the cells in the subcultures for increased tissue specific gene expression.

Full   Titl	e Citation Front	Review   Classification						Draw, Desi
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L26: Ent	ry 88 of 189		File:	PGPB		Aud	22,	2002

PGPUB-DOCUMENT-NUMBER: 20020114788

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020114788 A1

TITLE: Cell implantation therapy for neurological diseases or disorders

PUBLICATION-DATE: August 22, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE COUNTRY RULE-47

Isacson, Ole

Cambridge

MA

US

Kim, Kwang Soo

Lexington

MΑ

US

US-CL-CURRENT: 424/93.21; 435/368, 435/456

#### ABSTRACT:

Disclosed herein is a method for generating functional lineage-restricted progenitors from embryonic stem cells for obtaining donor cells of specific neuronal cell-fate, in sufficient quantities for the unmet cell transplantation need for treating patients with neurodegenerative diseases or disorders.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desi
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□ 89. Document ID: US 20020104114 A1

L26: Entry 89 of 189

File: PGPB

Aug 1, 2002

PGPUB-DOCUMENT-NUMBER: 20020104114

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020104114 A1

TITLE: Transgenic animals for screening therapeutic agents for brain tumors

PUBLICATION-DATE: August 1, 2002

INVENTOR-INFORMATION:

NAME

CTTY

STATE

COUNTRY

RULE-47

Chiu, Ing-Ming

Dublin

OH

US-CL-CURRENT: 800/18

# ABSTRACT:

A transgenic, non-human mammal useful for assessing the effect of candidate chemotherapeutic drugs on the growth of brain tumors in vivo is provided. Incorporated into the genome of the transgenic mammal, which preferably is a rodent, is a transgene which comprises a promoter comprising the nuclear factor binding region of the RR2 cis acting element of a fibroblast growth factor 1B (FGF1B) promoter. Operably linked to the promoter is reporter gene comprising a sequence which encodes the SV40 large T antigen. A transgenic, non-human mammal useful for identifying and isolating FGF1 producing brain cells. Incorporated into the genome of these transgenic animals is a transgene which comprises a promoter comprising the nuclear factor binding region of the RR2 cis acting element of an fibroblast growth factor 1B (FGF1B) promoter. Operably linked to the promoter is reporter gene comprising a sequence which encodes a protein or polypeptide other than an SV40 large T antigen. A method of obtaining neural stem cells from a sample of cells obtained from an animal is also provided. Such method comprises introducing the FGF1B-detector transgene into a sample of cells that have been obtained from the animal, and assaying for expression of the detectable marker in the cells, wherein cells that express the marker are neural stem cells. The cells which express the detectable marker can then be isolated from the population to provide a sub-population of neural

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw. Desc

☐ 90. Document ID: US 20020098582 A1

L26: Entry 90 of 189

File: PGPB

Jul 25, 2002

PGPUB-DOCUMENT-NUMBER: 20020098582

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020098582 A1

TITLE: Differentiated stem cells suitable for human therapy

PUBLICATION-DATE: July 25, 2002

INVENTOR-INFORMATION:

NAME

CTTY

STATE

COUNTRY RULE-47

Gold, Joseph D. Lebkowski, Jane S. San Francisco Portola Valley CA CA

US US

US-CL-CURRENT: 435/366; 424/93.21, 435/194

### ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

Full Title Citation Front Review	Classification Date	Reference	Sequences	Attachments	Claims	KMIC	Drawi Desc
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☐ 91. Document ID: US 20020090723 A1

L26: Entry 91 of 189

File: PGPB

Jul 11, 2002

PGPUB-DOCUMENT-NUMBER: 20020090723

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020090723 A1

TITLE: Techniques for growth and differentiation of human pluripotent stem cells

PUBLICATION-DATE: July 11, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Carpenter, Melissa K.

Castro Valley

:A US

Inokuma, Margaret S.

San Jose

CA US

CA

Xu, Chunhui

Cupertino

US

US-CL-CURRENT: 435/366; 435/368

### ABSTRACT:

This disclosure provides an improved system for culturing human pluripotent stem (pps) cells in the absence of feeder cells. The role of the feeder cells can be replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. Permanent cell lines are provided that can produce conditioned medium on a commercial scale. Methods have also been discovered to genetically alter pps cells by introducing the cells with a viral vector or DNA/lipid complex. The system described in this disclosure allows for bulk proliferation of pps cells for use in studying the biology of pps cell differentiation, and the production of important products for use in human therapy.

Full Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KOMC	Draw, Desi
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☐ 92. Document ID: US 20020090603 A1

L26: Entry 92 of 189

File: PGPB

Jul 11, 2002

PGPUB-DOCUMENT-NUMBER: 20020090603

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020090603 A1

TITLE: Methods of differentiating and protecting cells by modulating the P38/MEF2 pathway

PUBLICATION-DATE: July 11, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Lipton, Stuart A.

Rancho Santa Fe

CA

US

Okamoto, Shu-ichi

San Diego

CA

US

US-CL-CURRENT: 435/4; 435/372

### ABSTRACT:

The present invention provides a method of differentiating progenitor cells to produce a population containing protected neuronal cells. A method of the invention includes the steps of contacting the progenitor cells with a differentiating agent; and introducing into the progenitor cells a nucleic acid molecule encoding a MEF2 polypeptide or an active fragment thereof, thereby differentiating the progenitor cells to produce a population containing protected neuronal cells. In one embodiment, the MEF2 polypeptide is human MEF2C or an active fragment thereof.

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☐ 93. Document ID: US 20020086005 A1

L26: Entry 93 of 189 File: PGPB Jul 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020086005

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020086005 A1

TITLE: Tolerizing allografts of pluripotent stem cells

PUBLICATION-DATE: July 4, 2002

INVENTOR-INFORMATION:

STATE NAME CITY COUNTRY RULE-47

CA Chiu, Choy-Pik Cupertino CAUS Kay, Robert M. San Francisco

US-CL-CURRENT: 424/93.21; 424/93.7, 435/366

#### ABSTRACT:

This disclosure provides a system for overcoming HLA mismatch between an allograft derived from stem cells, and a patient being treated for tissue regeneration. A state of specific immune tolerance is induced in the patient, by administering a population of tolerizing cells derived from the stem cells. This allows the patient to accept an allograft of differentiated cells derived from the same source. This invention is important because it allows a single line of stem cells to act as a universal donor source for tissue regeneration in any patient, regardless of tissue type.

Full	Title Citation Front Review	Classification Date	Reference Sequences	Attachments Claims	KMMC   Drawn Desi
	94. Document ID: US	20020081724 A1			
L26:	Entry 94 of 189		File: PGPB	Jun	27, 2002

PGPUB-DOCUMENT-NUMBER: 20020081724

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020081724 A1

TITLE: Techniques for growth and differentiation of human pluripotent stem cells

PUBLICATION-DATE: June 27, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Carpenter, Melissa K.	Castro Valley	CA	US	
Funk, Walter D.	Hayward	CA	US	
Gold, Joseph D.	San Francisco	CA	US	
Inokuma, Margaret S.	San Jose	CA	US	
Xu, Chunhui	Cupertino	CA	US	

US-CL-CURRENT: 435/366; 435/354, 435/384

### ABSTRACT:

This disclosure provides an improved system for culturing human pluripotent stem (pps) cells in the absence of feeder cells. The role of the feeder cells can be replaced by supporting the culture on an extracellular matrix, and culturing the cells in a conditioned medium. Permanent cell lines are provided that can produce conditioned medium on a commercial scale. Methods have also been discovered to genetically alter pps cells by introducing the cells with a viral vector or DNA/lipid complex. The system described in this disclosure allows for bulk proliferation of pps cells for use in studying the biology of pps cell differentiation, and the production of important products for use in human therapy.

Full	Title Citation		Classification					KWAC	Drawi Desi
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Ĺ	95. Docum	ent ID: US 2	2002006804	5 A I					
L26:	Entry 95 of	189			File	: PGPB	Ju	n 6,	2002

PGPUB-DOCUMENT-NUMBER: 20020068045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020068045 A1

TITLE: Embryonic stem cells and neural progenitor cells derived therefrom

PUBLICATION-DATE: June 6, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Reubinoff, Benjamin Eithan Mevaseret-Zion IL
Pera, Martin Frederick Prahran AU
Ben-Hur, Tamir Ramat Sharet IL

US-CL-CURRENT: <u>424/93.7</u>; <u>435/368</u>

# ABSTRACT:

The present invention provides undifferentiated human embryonic stem cells, methods of cultivation and propagation and production of differentiated cells. In particular it relates to the production of human ES cells capable of yielding somatic differentiated cells in vitro, and committed progenitor cells such as neural progenitor cells capable of giving rise to mature somatic cells including neural cells and/or glial cells and uses thereof. The invention also provides methods that generate in vitro and in vivo models of controlled differentiation of ES cells towards the neural lineage. The model, and the cells that are generated along the pathway of neural differentiation may be used for the study of the cellular and molecular biology of human neural development, for the discovery of genes, growth factors, and differentiation factors that play a role in neural differentiation and regeneration, for drug discovery and for the development of screening assays for teratogenic, toxic and neuroprotective effects.

Full	Title   Citation   F	Frant Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Dés
	96. Docume	nt ID: US 2	0020045251	Al						
L26:	Entry 96 of	189			File:	PGPB		Apr	: 18,	2002

PGPUB-DOCUMENT-NUMBER: 20020045251

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020045251 A1

TITLE: COMMON NEURAL PROGENITOR FOR THE CNS AND PNS

PUBLICATION-DATE: April 18, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

RAO, MAHENDRA S. SALT LAKE CITY UT US

MUJTABA, TAHMINA SANDY UT US

US-CL-CURRENT:  $\underline{435}/\underline{325}$ ;  $\underline{435}/\underline{368}$ ,  $\underline{435}/\underline{373}$ ,  $\underline{435}/\underline{377}$ ,  $\underline{435}/\underline{383}$ ,  $\underline{435}/\underline{384}$ ,  $\underline{435}/\underline{387}$ ,

<u>435/391</u>, <u>435/395</u>, <u>435/402</u>

#### ABSTRACT:

A method of generating neural crest stem cells involves inducing neuroepithelial stem cells to differentiate in vitro into neural crest stem cells. Differentiation can be induced by replating the cells on laminin, withdrawing mitogens, or adding dorsalizing agents to the growth medium. Derivatives of the peripheral nervous system can be generated by inducing the neural crest stem cells to differentiate in vitro.

Full	Title Citation Front	Review C	lassification	Date	Reference	Sequences	Attachments	Claims	KMIC	Draw, Desc
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	97. Document ID	: US 200	20039789	<b>A</b> 1						
L26:	Entry 97 of 189				File:	PGPB		Ap	r 4,	2002

PGPUB-DOCUMENT-NUMBER: 20020039789

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020039789 A1

TITLE: Method for production of neuroblasts

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Gage, Fred H. La Jolla CA US
Ray, Jasodhara San Diego CA US

US-CL-CURRENT: 435/368

### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

# 98. Document ID: US 20020039724 A1

L26: Entry 98 of 189

File: PGPB

Apr 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020039724

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020039724 A1

TITLE: Neural progenitor cell populations

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Carpenter, Melissa K. Castro Valley CA US

US-CL-CURRENT: 435/4; 435/368

### ABSTRACT:

This invention provides populations of neural progenitor cells, differentiated neurons, glial cells, and astrocytes. The populations are obtained by culturing stem cell populations (such as embryonic stem cells) in a cocktail of growth conditions that initiates differentiation, and establishes the neural progenitor population. The progenitors can be further differentiated in culture into a variety of different neural phenotypes, including dopaminergic neurons. The differentiated cell populations or the neural progenitors can be generated in large quantities for use in drug screening and the treatment of neurological disorders.

Full Title Citation Front	Review Classification	Date Reference	Sequences	Attachments Claims	KMMC Draw, Desc

# ☐ 99. Document ID: US 20020037281 A1

L26: Entry 99 of 189

File: PGPB

Mar 28, 2002

PGPUB-DOCUMENT-NUMBER: 20020037281

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020037281 A1

TITLE: Methods of transducing neural cells using lentivirus vectors

PUBLICATION-DATE: March 28, 2002

### INVENTOR-INFORMATION:

THE THE OWN THE OWN THE TONE				
NAME	CITY	STATE	COUNTRY	RULE-47
Davidson, Beverly L.	North Liberty	IA .	US .	
Alisky, Joseph M.	Iowa City	IA	US	
Dubensky, Thomas W. JR.	Piedmont	CA	US ·	
Hughes, Stephanie M.	Iowa City	IA	US	
Jolly, Douglas	Encinitas	CA	US	
Sauter, Sybille L.	Del Mar	CA	US	

US-CL-CURRENT: 424/93.21; 435/368, 435/456

#### ABSTRACT:

Gene delivery vectors, such as, for example, recombinant FIV vectors, and methods of using such vectors are provided for use in transducing neural cells, such as neural progenitor cells, and cerebellar neurons, in particular, Purkinje cells.

Full	Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KARAC	Draw, Desc
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L26:	Entry	100 of 189	9			File:	PGPB		Mar	14,	2002

PGPUB-DOCUMENT-NUMBER: 20020031792

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020031792 A1

TITLE: Enriched central nervous system stem cell and progenitor cell populations, and methods for identifying, isolating and enriching for such populations

PUBLICATION-DATE: March 14, 2002

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Uchida, Nobuko	Palo Alto	CA	US	
Buck, David W.	Santa Clara	CA	US	
Weissman, Irving	Redwood City	CA	US	

US-CL-CURRENT: <u>435/7.21</u>; <u>435/368</u>

# ABSTRACT:

Enriched neural stem and progenitor cell populations, and methods for identifying, isolating and enriching for neural stem cells using reagent that bind to cell surface markers, are provided.

Full Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw De
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# Search Results - Record(s) 101 through 189 of 189 returned.

☐ 101. Document ID: US 20020028510 A1

Using default format because multiple data bases are involved.

L26: Entry 101 of 189

File: PGPB

Mar 7, 2002

Feb 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020028510

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020028510 A1

TITLE: Human cord blood as a source of neural tissue for repair of the brain and

spinal cord

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

STATE COUNTRY RULE-47 NAME CITY Spring Hill Sanberg, Paul FLUS Sanchez-Remos, Juan Tampa FLUS Willing, Alison Tampa FLUS Richard, Daniel D. Sedona ΑZ US

US-CL-CURRENT: 435/368

Full	Title	Citation Front R	eview	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draws Desc
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LJ	102.	Document ID:	US:	200200190	46 A						

File: PGPB

PGPUB-DOCUMENT-NUMBER: 20020019046

PGPUB-FILING-TYPE: new

L26: Entry 102 of 189

DOCUMENT-IDENTIFIER: US 20020019046 A1

TITLE: Direct differentiation of human pluripotent stem cells and characterization of

differentiated cells

PUBLICATION-DATE: February 14, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 Carpenter, Melissa K. Castro Valley CA US CA US Funk, Walter D. Hayward Thies, R. Scott Pleasanton CA US

US-CL-CURRENT: 435/368; 435/4, 435/91.1

### ABSTRACT:

This invention provides a system for efficiently producing differentiated cells from pluripotent cells, such as human embryonic stem cells. Rather than permitting the cells to form embryoid bodies according to established techniques, differentiation is effected directly in monolayer culture on a suitable solid surface. The cells are either plated directly onto a differentiation-promoting surface, or grown initially on the solid surface in the absence of feeder cells and then exchanged into a medium that assists in the differentiation process. The solid surface and the culture medium can be chosen to direct differentiation down a particular pathway, generating a cell population that is remarkably uniform. The methodology is well adapted to bulk production of committed precursor and terminally differentiated cells for use in drug screening or regenerative medicine.

Full	Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Drawy Desi
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L26:	Entry	103 of 189				Fil	e: PGPB		Fe	b 7,	2002

PGPUB-DOCUMENT-NUMBER: 20020016002

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020016002 A1

TITLE: Multipotent neural stem cells from peripheral tissues and uses thereof

PUBLICATION-DATE: February 7, 2002

### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Toma, Jean	Montreal		CA	
Akhavan, Mahnaz	Montreal		CA	
Fernandes, Karl J. L.	Montreal		CA	
Fortier, Mathieu	Orford		CA	
Miller, Freda	Montreal		CA	

US-CL-CURRENT: 435/368; 435/366

### ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

Citation   Front   Review	 •	· · · · · · · · · · · · · · · · · · ·	- · · · · · · · · · · · · · · · · · · ·	•		Draw Desi
 Document ID: US 104 of 189			: PGPB		31,	

PGPUB-DOCUMENT-NUMBER: 20020012903

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020012903 A1

TITLE: Method for isolating and purifying multipotential neural progenitor cells and multipotential neural progenitor cells

PUBLICATION-DATE: January 31, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Goldman, Steven A. South Salem NY US Okano, Hideyuki Osaka JP

US-CL-CURRENT: 435/4; 435/368

### ABSTRACT:

The present invention relates to a method of separating multipotential neural progenitor cells from a mixed population of cell types. This method includes selecting a promoter which functions selectively in the neural progenitor cells, introducing a nucleic acid molecule encoding a fluorescent protein under control of said promoter into all cell types of the mixed population of cell types, allowing only the neural progenitor cells, but not other cell types, within the mixed population to express said fluorescent protein, identifying cells of the mixed population of cell types that are fluorescent, which are restricted to the neural progenitor cells, and separating the fluorescent cells from the mixed population of cell types, wherein the separated cells are restricted to the neural progenitor cells. The present invention also relates to an isolated human musashi promoter and an enriched or purified preparation of isolated multipotential neural progenitor cells.

Full	Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC.	Draw, Desc
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	105.	Document ID	): US 2	2002000974	43 A	1		,			
L26:	Entry	105 of 189				File:	PGPB		Jan	24,	2002

PGPUB-DOCUMENT-NUMBER: 20020009743

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020009743 A1

TITLE: Neural progenitor cell populations

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Carpenter, Melissa K. Castro Valley CA US

US-CL-CURRENT: 435/6; 424/93.21, 435/368

# ABSTRACT:

This invention provides populations of neural progenitor cells, differentiated neurons, glial cells, and astrocytes. The populations are obtained by culturing stem cell populations (such as embryonic stem cells) in a cocktail of growth conditions

that initiates differentiation, and establishes the neural progenitor population. The progenitors can be further differentiated in culture into a variety of different neural phenotypes, including dopaminergic neurons. The differentiated cell populations or the neural progenitors can be generated in large quantities for use in drug screening and the treatment of neurological disorders.

Full	Title	Citation   Front   R	eview Classification	Date Reference	Sequences Attachm	ents Claims (	KMC	Drawi Desi
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	106.	Document ID:	US 2002000946	1 A1				
L26:	Entry	106 of 189		File:	PGPB	Jan	24,	2002

PGPUB-DOCUMENT-NUMBER: 20020009461

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020009461 A1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due to neurodegenerative diseases

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Isacson, Ole Cambridge MA US
Dinsmore, Jonathan Brookline MA US

US-CL-CURRENT: 424/193.1; 424/93.7, 435/325

### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

Full Title Citation Front Review Classification Date R	eference   Sequences   Attachments   CI	laims KMC Draw Desc
☐ 107. Document ID: US 20020006660 A1 L26: Entry 107 of 189	File: PGPB	Jan 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020006660

PGPUB-FILING-TYPE: new

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DOCUMENT-IDENTIFIER: US 20020006660 A1

TITLE: GENETICALLY-MODIFIED NEURAL PROGENITORS AND USES THEREOF

PUBLICATION-DATE: January 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47 SABATE, OLIVIER PARIS FR HORELLOU, PHILIPPE PARIS FR BUC-CARON, MARIE-HELENE PARIS FR PARIS FR MALLET, JACQUES

US-CL-CURRENT: 435/325; 514/44

### ABSTRACT:

The invention concerns human neural progenitor cells containing introduced genetic material encoding a product of interest, and their use for the treatment of neurodegenerative diseases.

Full 1	itle Citation	Front Review	Classification Date	Reference Se	quences	Attachments	Claims k	OMC	Draw, Desc
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П	08 Doc	ument ID: US 2	20020004039 A1						
L26: E	00. <b>200</b>								

PGPUB-DOCUMENT-NUMBER: 20020004039

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020004039 A1

TITLE: Methods for treating neurological deficits

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Reid, James Steven Berkeley CA US
Fallon, James H. Irvine CA US

US-CL-CURRENT: 424/93.7; 435/368

# ABSTRACT:

The present invention features methods and compositions for treating a patient who has a neurological deficit. The method can be carried out, for example, by contacting (in vivo or in culture) a neural progenitor cell of the patient's central nervous system (CNS) with a polypeptide that binds the epidermal growth factor (EGF) receptor and directing progeny of the proliferating progenitor cells to migrate en masse to a region of the CNS in which they will reside and function in a manner sufficient to reduce the neurological deficit. The method may include a further step in which the progeny of the neural precursor cells are contacted with a compound that stimulates differentiation.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Des

☐ 109. Document ID: US 20010055808 A1

L26: Entry 109 of 189

File: PGPB

Dec 27, 2001

PGPUB-DOCUMENT-NUMBER: 20010055808

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010055808 A1

TITLE: Use of collagenase in the preparation of neural stem cell cultures

PUBLICATION-DATE: December 27, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Uchida, Nobuko

Palo Alto

CA

US

US-CL-CURRENT: 435/368

### ABSTRACT:

The invention provides a method for using collagenase to dissociate neural stem cells in neural stem cell cultures. The collagenase treatment results in an increased cell viability and an increased number of proliferated neural stem cells over time.

	- UII	litte	Citation Front Review	Classification   L	Pate   Reference	pediferines	Auschneins	Claims	KOOL	Diami Dazi
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	$\Box$	110	Document ID: US	20010052124	`					
	ш	HO.	Document ID. US	20010032130	JAI	·				

PGPUB-DOCUMENT-NUMBER: 20010052136

PGPUB-FILING-TYPE: new

L26: Entry 110 of 189

DOCUMENT-IDENTIFIER: US 20010052136 A1

TITLE: Compositions and methods for producing and using homogenous neuronal cell

transplants

PUBLICATION-DATE: December 13, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

RULE-47

Dec 13, 2001

Lee, Virginia M. Y.

Philadelphia

PA

File: PGPB

US

COUNTRY

Trojanowski, John Q.

Philadelphia

PA

US

US-CL-CURRENT: 800/12; 424/93.21

# ABSTRACT:

Methods of treating individuals suspected of suffering from diseases, conditions or disorders of the Central Nervous System which comprise implanting stable, homogeneous

post-mitotic human neurons into the individual's brain are disclosed. Methods of treating individuals suspected of suffering from injuries, diseases, conditions or disorders characterized by nerve damage which comprise implanting stable, homogeneous post-mitotic human neurons at or near a site of said nerve damage. Pharmaceutical compositions comprising stable, homogeneous post-mitotic human neurons and a pharmaceutically acceptable medium are disclosed. Methods of generating non-human animal models of human CNS diseases, conditions or disorders which comprise implanting stable, homogeneous post-mitotic human neurons into the brain of a non-human animal are disclosed. Non-human animals comprising stable, homogeneous post-mitotic human neurons implanted in their brain are disclosed.

Full	Title	Citation Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desc
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L	111.	Document II	D; US:	2001004412	22 A I	ļ					
L26:	Entry	111 of 189				File	: PGPB		уои	22,	2001

PGPUB-DOCUMENT-NUMBER: 20010044122

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010044122 A1

TITLE: Enriched central nervous system stem cell and progenitor cell populations, and methods for identifying, isolating and enriching for such populations

PUBLICATION-DATE: November 22, 2001

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Buck, David W.	Heathfield	CA	GB	
Uchida, Nobuko	Palo Alto	CA	US	
Weissman, Irving	Redwood City		US	

US-CL-CURRENT: 435/7.21; 435/368

# ABSTRACT:

Enriched neural stem and progenitor cell populations, and methods for identifying, isolating and enriching for neural stem cells using reagent that bind to cell surface markers, are provided.

Full	Title	Citation Front Re	eview Classification	Date   Reference	Sequences /	Attachments	Claims	KMC	Drawi Desi
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	112.	Document ID:	US 2001004392	23 A1					
L26:	Entry	112 of 189		File	PGPB		Nov	22,	2001

PGPUB-DOCUMENT-NUMBER: 20010043923

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010043923 A1

TITLE: Mx-1 conditionally immortalized cells

PUBLICATION-DATE: November 22, 2001

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Schinstine, Malcolm	Ben Salem	PA .	US	
Shoichet, Molly S.	Toronto	RI	CA	
Gentile, Frank T.	Warwick	RI	US	
Hammang, Joseph P.	Barrington	PA	US	
Holland, Laura M.	Horsham	MA	US	
Cain, Brian M.	Everett	MA	US	
Doherty, Edward J.	Mansfield	RI	US	
Winn, Shelley R.	Smithfield		US	
Aebischer, Patrick	Lutry	•	СН	

US-CL-CURRENT: 424/93.21

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

Full	Title	Citation Front Review Clas	sification   Date	Reference :	Sequences	Attachments	Claims	KWMC	Draw, Des
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	113.	Document ID: US 200	10034061 A1						
L26:	Entry	113 of 189		File:	PGPB		Oct	25,	2001

PGPUB-DOCUMENT-NUMBER: 20010034061

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010034061 A1

TITLE: Methods for isolation and activation of, and control of differentiation from,

stem and progenitor cells

PUBLICATION-DATE: October 25, 2001

# INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Csete, Marie	South Pasadena	CA	US	
Doyle, John	South Pasadena	CA	US	
Wold, Barbara	San Marino	CA	US	

US-CL-CURRENT: 435/377; 435/4, 435/455

# ABSTRACT:

The present invention provides a method of isolating, maintaining, and/or enriching for stem or progenitor cells derived from diverse organ or tissue sources. The

invention specifically teaches that these can be accomplished by the controlled use of subatmospheric oxygen culture, and that the precise oxygen level or levels must be determined empirically and/or by reference to physiologic levels within intact functioning organ or tissue.

Full Title Citation Front Review Classification Date Reference Sequences Attachments Claims KMC Draw Desc

☐ 114. Document ID: US 20010033834 A1

L26: Entry 114 of 189

File: PGPB

Oct 25, 2001

PGPUB-DOCUMENT-NUMBER: 20010033834

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010033834 A1

TITLE: Pleuripotent stem cells generated from adipose tissue-derived stromal cells

and uses thereof

PUBLICATION-DATE: October 25, 2001

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Wilkison, William O. Bahama NC US Gimble, Jeffrey Chapel Hill NC US

US-CL-CURRENT: 424/93.7; 424/93.21, 435/325, 435/366, 435/368, 435/372

# ABSTRACT:

The invention is in the area of pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof. In particular, the invention includes isolated adipose tissue derived stromal cells that have been induced to express at least one phenotypic characteristic of a neuronal, astroglial, hematopoietic progenitor, or hepatic cell. The invention also includes an isolated adipocyte tissue-derived stromal cell that has been dedifferentiated such that there is an absence of adipocyte phenotypic markers.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw Desi

☐ 115. Document ID: US 20010029045 A1

L26: Entry 115 of 189 File: PGPB Oct 11, 2001

PGPUB-DOCUMENT-NUMBER: 20010029045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010029045 A1

TITLE: Lineage restricted glial precursors from the central nervous system

PUBLICATION-DATE: October 11, 2001

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Rao, Mahendra S. Salt Lake City UT US
Noble, Mark Brighton NY US
Mayer-Proschel, Margot Pittsford NY US

US-CL-CURRENT: 435/325; 424/93.7

### ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

Full Title	Citation Front Review Classification	Date Reference Sequences Attachr	nents   Claims   KMC   Draw. Desc
116.	Document ID: US 200100076		
L26: Entry	116 of 189	File: PGPB	Jul 12, 2001

PGPUB-DOCUMENT-NUMBER: 20010007657
PGPUB-FILING-TYPE: new-utility

DOCUMENT-IDENTIFIER: US 20010007657 A1

TITLE: Compositions and methods for manipulating glial progenitor cells and treating neurological deficits

PUBLICATION-DATE: July 12, 2001

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47
Reid, James Steven Berkeley CA US
Fallon, James H. Irvine CA US

US-CL-CURRENT: 424/93.7

### ABSTRACT:

The invention provides compositions and methods for attracting glial and neuronal progenitor cells and their progeny to desired sites within the central nervous system tissue. These compositions and methods can also be used to induce directed differentiation of these cells. By providing various ways to generate new glial and neuronal cells from endogenous progenitor cells, the invention also provides methods for inducing regeneration of tissues and neurological function, and, indeed, generating new phenotypes and capabilities. Thus, the invention features methods and compositions for ameliorating neurological deficits, including inherited disorders, trauma, infections and the like.

Full Title Citation Front Review	Classification Date	Reference Sequer	ices Attachments	Claims KMC Draw. (	)es:

# ☐ 117. Document ID: US 20010001662 A1

L26: Entry 117 of 189

File: PGPB

May 24, 2001

PGPUB-DOCUMENT-NUMBER: 20010001662 PGPUB-FILING-TYPE: new-utility

DOCUMENT-IDENTIFIER: US 20010001662 A1

TITLE: Neural transplantation using pluripotent neuroepithelial cells

PUBLICATION-DATE: May 24, 2001

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Sinden, John	London		GB ·	
Gray, Jeffrey A.	London		GB	
Hodges, Helen	London		GB	
Kershaw, Timothy	London		GB	
Rashid-Doubell, Fiza	Oxford		GB	

US-CL-CURRENT: 424/93.21; 424/93.7

#### ABSTRACT:

The subject invention pertains to a novel method of correction of behavioral and/or psychological deficits made possible by the intracerebral transplantation of pluripotent neuroepithelial cells. Cells, cell lines, pharmaceutical preparations, medicaments, methods for the production and maintenance of the cell lines for use in the method of the invention are encompassed by the invention.

Full	Title	Citation Front Re	view Classification	Date Reference	Sequences	Attachments Claims	KMMC   Draw, Desi
			US 6787356 B1		, ,	an mmaaaaaaaan ah	manasanasanamanasanas
L26:	Entry	118 of 189		Fil	e: USPT	Se	ep 7, 2004

US-PAT-NO: 6787356

DOCUMENT-IDENTIFIER: US 6787356 B1

TITLE: Cell expansion system for use in neural transplantation

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Studer; Lorenz New York NY McKay; Ron D. Bethesda MD

US-CL-CURRENT: 435/377; 424/93.21, 435/325, 435/384, 514/44

# ABSTRACT:

The invention provides a method of culturing cells which includes a proliferating step in which the number of precursor cells is expanded and a differentiating step in

which the expanded precursor cells develop into neuronal cells. The proliferating step includes the step of incubating the precursor cells in proliferating medium which includes basic fibroblast growth factor (bFGF). The differentiating step includes incubating the precursor cells in differentiation media in a manner effective to form a cellular aggregate that is not adhered to any surface of the incubation vessel. In a preferred embodiment, the cells are incubated in a roller tube. The differentiation media can also include at least one differentiating agent. The invention also provides a method for treating a neurological disorder, such as Parkinson's disease, a method of introducing a gene product into a brain of a patient, an assay for neurologically active substances, and a cell culture.

23 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 8

Full	Title	Citation Front Revie				Claims	KVMC	Dram Desc
	119.	Document ID: U						
L26:	Entry	119 of 189		File	e: USPT	Se	n 7.	2004

US-PAT-NO: 6787355

DOCUMENT-IDENTIFIER: US 6787355 B1

TITLE: Multipotent neural stem cells from peripheral tissues and uses thereof

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Miller; Freda D. Montreal CA
Gloster; Andrew Saskatoon CA
Toma; Jean Montreal CA

US-CL-CURRENT: 435/377; 435/325, 435/375, 435/378, 435/383

### ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

8 Claims, 0 Drawing figures Exemplary Claim Number: 1

<u> </u>	Citation Front Review	·	•			Claims	KWMC	Draw, Des
	Document ID: US			·			anne de la company de la compa	
L26: Entry	120 of 189			Fil	e: USPT	Se	p. 7,	2004

US-PAT-NO: 6787353

DOCUMENT-IDENTIFIER: US 6787353 B1

TITLE: Lineage-restricted neuronal precursors and methods of isolation

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME

CITY STATE

\_\_\_\_

ZIP CODE

COUNTRY

Rao; Mahendra S.

Salt Lake City

UT

Mayer-Proschel; Margot

Sandy

 $\mathbf{U}\mathbf{T}$ 

Kalyani; Anjali J.

Salt Lake City

UT

US-CL-CURRENT: 435/368; 435/377

### ABSTRACT:

A self-renewing restricted stem cell population has been identified in developing (embryonic day 13.5) spinal cords that can differentiate into multiple neuronal phenotypes, but cannot differentiate into glial phenotypes. This neuronal-restricted precursor (NRP) expresses highly polysialated or embryonic neural cell adhesion molecule (E-NCAM) and is morphologically distinct from neuroepithelial stem cells (NEP cells) and spinal glial progenitors derived from embryonic day 10.5 spinal cord. NRP cells self renew over multiple passages in the presence of fibroblast growth factor (FGF) and neurotrophin 3 (NT-3) and express a characteristic subset of neuronal epitopes. When cultured in the presence of RA and the absence of FGF, NRP cells differentiate into GABAergic, glutaminergic, and cholinergic immunoreactive neurons. NRP cells can also be generated from multipotent NEP cells cultured from embryonic day 10.5 neural tubes. Clonal analysis shows that E-NCAM immunoreactive NRP cells arise from an NEP progenitor cell that generates other restricted CNS precursors. The NEP-derived E-NCAM immunoreactive cells undergo self renewal in defined medium and differentiate into multiple neuronal phenotypes in mass and clonal culture. Thus, a direct lineal relationship exists between multipotential NEP cells and more restricted neuronal precursor cells present in vivo at embryonic day 13.5 in the spinal cord. Methods for treating neurological diseases are also disclosed.

7 Claims, 14 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 10

Full Title Citation Front Review	Classification Date	Reference	Clai	ms KMC Draw Desc
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# ☐ 121. Document ID: US 6777233 B2

L26: Entry 121 of 189

File: USPT

Aug 17, 2004

US-PAT-NO: 6777233

DOCUMENT-IDENTIFIER: US 6777233 B2

TITLE: Cultures of human CNS Neural stem cells

DATE-ISSUED: August 17, 2004

INVENTOR-INFORMATION:

NAME

Y STATE ZIP CODE

COUNTRY

Carpenter; Melissa

Foster City

CA

US-CL-CURRENT: 435/368; 435/377

#### ABSTRACT:

The invention provides a method for determining the effect of a biological agent comprising contacting a cell culture with a biological agent. The cell culture of the invention contains a culture medium containing one or more preselected growth factors effective for inducing multipotent central nervous system (CNS) neural stem cell proliferation. The cell culture also contains, suspended in the culture medium, human multipotent CNS neural stem cells that are derived from primary CNS neural tissue that have a doubling rate faster than 30 days.

2 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full	Title	Citation Front Review Classification D	ate Reference		Claims	KMC	Draw, Desi
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	122.	Document ID: US 6767738 B1					
L26:	Entry	122 of 189	File	: USPT	Jul	27,	2004

US-PAT-NO: 6767738

DOCUMENT-IDENTIFIER: US 6767738 B1

TITLE: Method of isolating adult mammalian CNS-derived progenitor stem cells using density gradient centrifugation

DATE-ISSUED: July 27, 2004

# INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gage; Fred H.	La Jolla	CA		
Palmer; Theo	San Carlos	CA		
Safar; Francis G.	Irvine	CA		
Takahashi; Jun	Kyoto			JP
Takahashi; Masayo	Kyoto		•	JP

US-CL-CURRENT: 435/325; 435/366, 435/368, 435/378

# ABSTRACT:

The present invention is directed to methods of repairing damaged or diseased, specialized or differentiated tissue in mature animals, particularly neuronal tissue such as retinas. In particular, the invention relates to transplantation of adult, hippocampus-derived progenitor cells into a selected neural tissue site of a recipient. These cells can functionally integrate into mature and immature neural tissue. The invention encompasses, in one aspect, repopulating a retina of a dystrophic animal with neurons, by injecting clonally derived, adult central nervous system derived stem cells (ACSC) derived from a healthy donor animal into an eye of the dystrophic recipient. Herein disclosed is the first successful and stable integration of clonally derived ACSC into same-species but different strain recipients (e. g., Fischer rat-derived adult hippocampal derived progenitor cells (AHPCs) into dystrophic RCS rats). Surprisingly, AHPCs were also found to integrate successfully into a xenogeneic recipient (e.g., rat AHPCs into the retina of dystropic rd-I mice).

13 Claims, O Drawing figures Exemplary Claim Number: 1

Full Title Citation Front Review Classification Date Reference

aims KWC Draw. Des

☐ 123. Document ID: US 6749850 B1

L26: Entry 123 of 189

File: USPT

Jun 15, 2004

US-PAT-NO: 6749850

DOCUMENT-IDENTIFIER: US 6749850 B1

TITLE: Methods, compositions and kits for promoting recovery from damage to the

central nervous system

DATE-ISSUED: June 15, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Finkelstein; Seth P.

Needham

MA

Snyder; Evan Y.

Jamaica Plain

MA

US-CL-CURRENT: 424/93.7; 424/93.1, 514/12

#### ABSTRACT:

The present application relates to methods, kits and compositions for improving a subject's recovery from CNS injury. In certain aspects, methods of the invention comprise administering to a subject cells and a neural stimulant. Recovery may be manifest by improvements in sensorimotor or cognitive abilities, e.g., improved limb movement and control or improved speech capability. In certain embodiments, subject methods can be used as part of a treatment for damage resulting from ischemia, hypoxia or trauma.

7 Claims, 10 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

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124. Document ID: US 6734015 B1

L26: Entry 124 of 189

File: USPT

May 11, 2004

Claims KMC Draw Desc

US-PAT-NO: 6734015

DOCUMENT-IDENTIFIER: US 6734015 B1

TITLE: Isolation of lineage-restricted neuronal precursors

Title Citation Front Review Classification Date Reference

DATE-ISSUED: May 11, 2004

INVENTOR-INFORMATION:

NAME

STATE ZIP CODE

COUNTRY

Rao; Mahendra S.

Salt Lake City

UT

Mayer-Proschel; Margot

Sandy

 $\mathbf{U}\mathbf{T}$ 

US-CL-CURRENT: 435/368; 435/325

### ABSTRACT:

A self-renewing restricted stem cell population has been identified in developing (embryonic day 13.5) spinal cords that can differentiate into multiple neuronal phenotypes, but cannot differentiate into glial phenotypes. This neuronal-restricted precursor (NRP) expresses highly polysialated or embryonic neural cell adhesion molecule (E-NCAM) and is morphologically distinct from neuroepithelial stem cells (NEP cells) and spinal glial progenitors derived from embryonic day 10.5 spinal cord. NRP cells self renew over multiple passages in the presence of fibroblast growth factor (FGF) and neurotrophin 3 (NT-3) and express a characteristic subset of neuronal epitopes. When cultured in the presence of RA and the absence of FGF, NRP cells differentiate into GABAergic, glutaminergic, and cholinergic immunoreactive neurons. NRP cells can also be generated from multipotent NEP cells cultured from embryonic day 10.5 neural tubes. Clonal analysis shows that E-NCAM immunoreactive NRP cells arise from an NEP progenitor cell that generates other restricted CNS precursors. The NEP-derived E-NCAM immunoreactive cells undergo self renewal in defined medium and differentiate into multiple neuronal phenotypes in mass and clonal culture. Thus, a direct lineal relationship exists between multipotential NEP cells and more restricted neuronal precursor cells present in vivo at embryonic day 13.5 in the spinal cord.

1 Claims, 1 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 1

Full	Title	Citation Front	Review	Classification	Date	Reference		Claims	ROMO	Draw Desi
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	125.	Document II	D: US	6680198 B	1					
L26:	Entry	125 of 189				File	: USPT	Jan	20,	2004

US-PAT-NO: 6680198

DOCUMENT-IDENTIFIER: US 6680198 B1

TITLE: Engraftable human neural stem cells

DATE-ISSUED: January 20, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Snyder; Evan Y. Jamaica Plain MA Wolfe; John H. Philadelphia PA

Kim; Seung U. Vancouver CA

US-CL-CURRENT: 435/368; 424/93.7

### ABSTRACT:

Stable clones of neural stem cells (NSCs) have been isolated from the human fetal telencephalon. In vitro, these self-renewing clones (affirmed by retroviral insertion site) can spontaneously give rise to all 3 fundamental neural cell types (neurons, oligodendrocytes, astrocytes). Following transplantation into germinal zones of the developing newborn mouse brain, they, like their rodent counterparts, can participate in aspects of normal development, including migration along well-established migratory pathways to disseminated CNS regions, differentiation into multiple

developmentally- and regionally-appropriate cell types in response to microenvironmental cues, and non-disruptive, non-tumorigenic interspersion with host progenitors and their progeny. Readily genetically engineered prior to transplantation, human NSCs are capable of expressing foreign transgenes in vivo in these disseminated locations. Further supporting their potential for gene therapeutic applications, the secretory products from these NSCs can cross-correct a prototypical genetic metabolic defect in abnormal neurons and glia in vitro as effectively as do murine NSCs. Finally, human cells appear capable of replacing specific deficient neuronal populations in a mouse model of neurodegeneration and impaired development, much as murine NSCs could. Human NSCs may be propagated by a variety of means--both epigenetic (e.g., chronic mitogen exposure) and genetic (transduction of the propagating gene vmyc) -- that are comparably safe (vmyc is constitutively downregulated by normal developmental mechanisms and environmental cues) and effective in yielding engraftable, migratory clones, suggesting that investigators may choose the propagation technique that best serves the demands of a particular research or clinical problem. All clones can be cryopreserved and transplanted into multiple hosts in multiple settings.

2 Claims, 53 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 9

Fuli	Title	Citation Front Review Classification	Date Reference	CI	aims KWC Dra	im Desi
					•	
		Document ID: US 6677307 B2			***************************************	***************************************
L26:	Entry	126 of 189	File:	USPT	Jan 13, 200	04

US-PAT-NO: 6677307

DOCUMENT-IDENTIFIER: US 6677307 B2

TITLE: TGF-.alpha. polypeptides, functional fragments and methods of use therefor

DATE-ISSUED: January 13, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Twardzik; Daniel R. Bainbridge Island WA Pernet; Andre Lake Forest Felker; Thomas S. Vashon WA Paskell; Stefan Bainbridge Island WA Reno; John M. Brier

US-CL-CURRENT: 514/12; 530/300, 530/402

# ABSTRACT:

Disclosed are TGF-60 mimetics that PEGylated TGF-.alpha. polypeptides and PEGylated TGF-60 related polypetides or fragments thereof.

5 Claims, 13 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 8

Full Title Citation Front Review Classification Date Reference Communication Claims KWIC Draw. D	)es:
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# ☐ 127. Document ID: US 6667176 B1

L26: Entry 127 of 189

File: USPT

Dec 23, 2003

US-PAT-NO: 6667176

DOCUMENT-IDENTIFIER: US 6667176 B1

TITLE: cDNA libraries reflecting gene expression during growth and differentiation of

human pluripotent stem cells

DATE-ISSUED: December 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Funk; Walter D.	Hayward	CA		
Carpenter; Melissa K.	Foster City	CA		
Gold; Joseph D.	San Francisco	CA		
Inokuma; Margaret S.	San Jose	CA		
Xu: Chunhui	Cupertino	CA		

US-CL-CURRENT: 435/363; 435/320.1, 435/366, 435/377, 536/23.1

### ABSTRACT:

This disclosure provides a system for obtaining expression libraries from primate pluripotent stem (pPS) cells. pPS cells can be maintained in vitro without requiring a layer of feeder cells to inhibit differentiation. The role of the feeder cells is replaced by several other culture conditions provided in a suitable combination. Conditions that promote pPS cell growth without differentiation include supporting the culture on an extracellular matrix, and culturing the cells in a medium conditioned by another cell type. The cDNA libraries from such cultures are devoid of transcripts of feeder cell origin, relatively uncontaminated by transcripts from differentiated cells, and can have a high proportion of full-length transcripts. Subtraction libraries can also be produced that are enriched for transcripts modulated during differentiation.

27 Claims, 11 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 10

Full Title Citation Front Review Classifica	tion Date Reference Commission State of	Claims KMC Draw Desc
☐ 128. Document ID: US 666715	6 B2	
L26: Entry 128 of 189	File: USPT	Dec 23, 2003

US-PAT-NO: 6667156

DOCUMENT-IDENTIFIER: US 6667156 B2

TITLE: Diagnosis and treatment of neuroectodermal tumors

DATE-ISSUED: December 23, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Lyons; Susan A. Birmingham AL Sontheimer; Harald W. Birmingham AL

US-CL-CURRENT: 435/7.23; 435/7.1, 436/63, 436/64, 436/813

# ABSTRACT:

The present invention provides fusion proteins for the detection and treatment of neuroectodermal tumors. Previous work demonstrated that chlorotoxin is specific for glial-derived or meningioma-derived tumor cells. The current invention has extended the use of chlorotoxin-cytotoxin fusion proteins to treat the whole class neuroectodermal tumors such as gliomas, meningiomas, ependymonas, medulloblastomas, neuroblastomas, gangliomas, pheochromocytomas, melanomas, PPNET's, small cell carcinoma of the lung, Ewing's sarcoma, and metastatic tumors in the brain. Also, diagnostic methods are provided for screening neoplastic neuroectodermal tumors.

18 Claims, 15 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 15

Full	Title	Citation Front	Review	Classification	Date	Reference	Claims	комс	Draw, Desi
					***************************************		 		
	129.	Document I	D: US	6638763 B	1				

12). Bootiment 13. CS 0030703 B

L26: Entry 129 of 189

File: USPT

Oct 28, 2003

US-PAT-NO: 6638763

DOCUMENT-IDENTIFIER: US 6638763 B1

\*\* See image for <u>Certificate of Correction</u> \*\*

TITLE: Isolated mammalian neural stem cells, methods of making such cells

DATE-ISSUED: October 28, 2003

### INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Steindler; Dennis A. Memphis TNLaywell; Eric D. Memphis TN Kukekou; Valery G. Memphis TN Thomas; L. Brannon Johnson City TN

US-CL-CURRENT: 435/368; 435/325, 435/377, 435/384

# ABSTRACT:

Using a novel culture approach, previously unknown populations of neural progenitor cells have been found within an adult mammalian brain. By limiting cell-cell contact, dissociated adult brain yields at least two types of cell aggregates. These aggregates or clones of stem/precursor cells can be generated from adult brain tissue with significantly long postmortem intervals. Both neurons and glia arise from stem/precursor cells of these cultures, and the cells can survive transplantation to the adult mammalian brain.

1 Claims, 7 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full Title Citation Front Review Classification Date Reference Common Claims KMC Draw Des

☐ 130. Document ID: US 6610540 B1

L26: Entry 130 of 189

File: USPT

Aug 26, 2003

US-PAT-NO: 6610540

DOCUMENT-IDENTIFIER: US 6610540 B1

TITLE: Low oxygen culturing of central nervous system progenitor cells

DATE-ISSUED: August 26, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Csete; Marie Ann Arbor MΙ Doyle; John South Pasadena CA Wold; Barbara J. San Marino CA McKay; Ron Bethesda MD NY Studer; Lorenz New York

US-CL-CURRENT: 435/375; 435/325, 435/352, 435/368, 435/377, 435/4

# ABSTRACT:

The present invention relates to the growth of cells in culture under conditions that promote cell survival, proliferation, and/or cellular differentiation. The present inventors have found that proliferation was promoted and apoptosis reduced when cells were grown in lowered oxygen as compared to environmental oxygen conditions traditionally employed in cell culture techniques. Further, the inventors found that differentiation of precursor cells to specific fates also was enhanced in lowered oxygen where a much greater number and fraction of dopaminergic neurons were obtained when mesencephalic precursors were expanded and differentiated in lowered oxygen conditions. Thus at more physiological oxygen levels the proliferation and differentiation of CNS precursors is enhanced, and lowered oxygen is a useful adjunct for ex vivo generation of specific neuron types. Methods and compositions exploiting these findings are described.

11 Claims, 22 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 14

Full	Title	Citation Front R	eview Classification	Date	Reference	Tari	Claims	KMC Draw	. Des
			US 6599695 B2						
L26:	Entry	131 of 189			File:	USPT	Ju]	29, 2003	3

US-PAT-NO: 6599695

DOCUMENT-IDENTIFIER: US 6599695 B2

TITLE: Method for assaying for early gene expression in neuroblasts

DATE-ISSUED: July 29, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA 92037 Ray; Jasodhara San Diego CA 92130

US-CL-CURRENT: 435/4; 435/29, 435/6, 435/7.1, 435/7.2, 435/7.21

#### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

4 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full	Title	Citation Front Review Classification C	Date Refe	rence		,	Claims	KWIC	Diam Desi
	132.	Document ID: US 6589728 B2							
L26:	Entry	132 of 189		File:	USPT		Ju	18,	2003

US-PAT-NO: 6589728

DOCUMENT-IDENTIFIER: US 6589728 B2

TITLE: Methods for isolation and activation of, and control of differentiation from,

stem and progenitor cells

DATE-ISSUED: July 8, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Csete; Marie South Pasadena CA
Doyle; John South Pasadena CA
Wold; Barbara San Marino CA

US-CL-CURRENT: 435/4; 435/375, 435/377

# ABSTRACT:

The present invention provides a method of isolating, maintaining, and/or enriching for stem or progenitor cells derived from diverse organ or tissue sources. The invention specifically teaches that these can be accomplished by the controlled use of subatmospheric oxygen culture, and that the precise oxygen level or levels must be determined empirically and/or by reference to physiologic levels within intact functioning organ or tissue.

28 Claims, 0 Drawing figures

Title Citation Front Review Classification Date Reference

Claims KWIC Draw Desc

☐ 133. Document ID: US 6576464 B2

L26: Entry 133 of 189

File: USPT

Jun 10, 2003

US-PAT-NO: 6576464

DOCUMENT-IDENTIFIER: US 6576464 B2

TITLE: Methods for providing differentiated stem cells

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE ZIP CODE COUNTRY

Gold; Joseph D.

San Francisco

CA

Lebkowski; Jane S.

Portola Valley

CA

US-CL-CURRENT:  $\underline{435}/\underline{325}$ ;  $\underline{536}/\underline{23.1}$ ,  $\underline{536}/\underline{23.4}$ ,  $\underline{536}/\underline{24.1}$ ,  $\underline{536}/\underline{25.5}$ 

#### ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

30 Claims, 10 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 10

Claims KMC Draw Desc

☐ 134. Document ID: US 6562619 B1

L26: Entry 134 of 189

File: USPT

May 13, 2003

US-PAT-NO: 6562619

DOCUMENT-IDENTIFIER: US 6562619 B1

TITLE: Differentiation of human embryonic germ cells

Full Title Citation Front Review Classification Date Reference

DATE-ISSUED: May 13, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gearhart; John D. Baltimore MD Shamblott; Michael Joseph Baltimore MD

US-CL-CURRENT: 435/366; 424/93.21, 435/325

### ABSTRACT:

Primordial germ cells isolated from human embryonic tissue, such as from the gonadal ridges of human embryo, are disclosed. The primordial germ cells are cultured resulting in cells that resemble embryonic stem cells or embryonic germ cells in morphology and pluripotency. The cells are maintained several months in culture and can be genetically manipulated using transgenic technology to insert heterologous genetic material.

28 Claims, 10 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full	Title	Citation Front R	· · ·	assification	•		 Claims	KMMC	Draw, Desi
		Document ID:				e: USPT			2003

US-PAT-NO: 6541255

DOCUMENT-IDENTIFIER: US 6541255 B1

TITLE: Engraftable human neural stem cells

DATE-ISSUED: April 1, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Snyder; Evan Y. Jamaica Plain MA Wolfe; John H. Philadelphia PA

Kim; Seung U. Vancouver CA

US-CL-CURRENT: 435/368; 514/44

# ABSTRACT:

Stable clones of neural stem cells (NSCs) have been isolated from the human fetal telencephalon. In vitro, these self-renewing clones (affirmed by retroviral insertion site) can spontaneously give rise to all 3 fundamental neural cell types (neurons, oligodendrocytes, astrocytes). Following transplantation into germinal zones of the developing newborn mouse brain, they, like their rodent counterparts, can participate in aspects of normal development, including migration along well-established migratory pathways to disseminated CNS regions, differentiation into multiple developmentally- and regionally-appropriate cell types in response to microenvironmental cues, and non-disruptive, non-tumorigenic interspersion with host progenitors and their progeny. Readily genetically engineered prior to transplantation, human NSCs are capable of expressing foreign transgenes in vivo in these disseminated locations. Further supporting their potential for gene therapeutic applications, the secretory products from these NSCs can cross-correct a prototypical genetic metabolic defect in abnormal neurons and glia in vitro as effectively as do

murine NSCs. Finally, human cells appear capable of replacing specific deficient neuronal populations in a mouse model of neurodegeneration and impaired development, much as murine NSCs could. Human NSCs may be propagated by a variety of means—both epigenetic (e.g., chronic mitogen exposure) and genetic (transduction of the propagating gene vmyc)—that are comparably safe (vmyc is constitutively downregulated by normal developmental mechanisms and environmental cues) and effective in yielding engraftable, migratory clones, suggesting that investigators may choose the propagation technique that best serves the demands of a particular research or clinical problem All clones can be cryopreserved and transplanted into multiple hosts in multiple settings.

4 Claims, 53 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

Full Title	Citation Front Re	eview Classification	Date   Reference	e a sur	Claims K	WC	Draw Desc
□ 136.	Document ID:	US 6528306 B1			,		
L26: Entry	136 of 189	•	Fi	le: USPT	Mar	4,	2003

US-PAT-NO: 6528306

DOCUMENT-IDENTIFIER: US 6528306 B1

TITLE: Engraftable human neural stem cells

DATE-ISSUED: March 4, 2003

# INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Snyder; Evan Y. Jamaica Plain MA
Wolfe; John H. Philadelphia PA
Kim; Seung U. Vancouver CA

US-CL-CURRENT: 435/368; 435/455

# ABSTRACT:

Stable clones of neural stem cells (NSCs) have been isolated from the human fetal telencephalon. In vitro, these self-renewing clones (affirmed by retroviral insertion site) can spontaneously give rise to all 3 fundamental neural cell types (neurons, oligodendrocytes, astrocytes). Following transplantation into germinal zones of the developing newborn mouse brain, they, like their rodent counterparts, can participate in aspects of normal development, including migration along well-established migratory pathways to disseminated CNS regions, differentiation into multiple developmentally- and regionally-appropriate cell types in response to microenvironmental cues, and non-disruptive, non-tumorigenic interspersion with host progenitors and their progeny. Readily genetically engineered prior to transplantation, human NSCs are capable of expressing foreign transgenes in vivo in these disseminated locations. Further supporting their potential for gene therapeutic applications, the secretory products from these NSCs can cross-correct a prototypical genetic metabolic defect in abnormal neurons and glia in vitro as effectively as do murine NSCs. Finally, human cells appear capable of replacing specific deficient neuronal populations in a mouse model of neurodegeneration and impaired development, much as murine NSCs could. Human NSCs may be propagated by a variety of means--both epigenetic (e.q., chronic mitogen exposure) and genetic (transduction of the propagating gene vmyc) -- that are comparably safe (vmyc is constitutively

downrequiated by normal developmental mechanisms and environmental cues) and effective in yielding engraftable, migratory clones, suggesting that investigators may choose the propagation technique that best serves the demands of a particular research or clinical problem All clones can be cryopreserved and transplanted into multiple hosts in multiple settings.

3 Claims, 53 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

Full Title Citation Front Review Classification Date Reference Claims KWC Draw Des ☐ 137. Document ID: US 6498018 B1 L26: Entry 137 of 189 File: USPT Dec 24, 2002

US-PAT-NO: 6498018

DOCUMENT-IDENTIFIER: US 6498018 B1

TITLE: Cultures of human CNS neural stem cells

DATE-ISSUED: December 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Foster City Carpenter; Melissa CA

US-CL-CURRENT: 435/29; 435/368

### ABSTRACT:

The invention provides a method for determining the effect of a biological agent comprising contacting a cell culture with a biological agent. The cell culture of the invention contains a culture medium containing one or more preselected growth factors effective for inducing multipotent central nervous system (CNS) neural stem cell proliferation. The cell culture also contains, suspended in the culture medium, human multipotent CNS neural stem cells that are derived from primary CNS neural tissue that have a doubling rate faster than 30 days.

4 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full	Title	Citation Front Re	eview Classification	Date	Reference		Claims	KWC	Draws Desc
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	138.	Document ID:	US 6497872 B	1					
L26:	Entry	138 of 189			File	: USPT	Dec	24,	2002

US-PAT-NO: 6497872

DOCUMENT-IDENTIFIER: US 6497872 B1

TITLE: Neural transplantation using proliferated multipotent neural stem cells and their progeny

DATE-ISSUED: December 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Weiss; Samuel Alberta CA
Reynolds; Brent Alberta CA

Hammang; Joseph P. Barrington RI Baetge; E. Edward Barrington RI

US-CL-CURRENT: 424/93.1; 424/93.2, 424/93.21

#### ABSTRACT:

The invention provides methods of transplanting multipotent neural stem cell progeny to a host by obtaining a population of cells derived from mammalian neural tissue containing at least one multipotent CNS multipotent neural stem cell; culturing the neural stem cell in a culture medium containing one or more growth factors which induce multipotent neural stem cell proliferation; inducing proliferation of the multipotent neural stem cell to produce neural stem cell progeny which includes multipotent neural stem cell progeny cells; and transplanting the multipotent neural stem cell progeny to the host. Also provided are methods of transplanting neural stem cell progeny to a host by obtaining an in vitro cell culture containing CNS neural stem cells where one or more cells in the culture (i) proliferates in a culture medium supplemented with one or more mitrogens, (ii) retains the capacity for renewed proliferation, and (iii) maintains the multipotential capacity, under suitable culture conditions, to differentiate into neurons, astrocytes, and oligodendrocytes; and transplanting the one or more cells to the hose.

32 Claims, 9 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full Title	Citation Front Revi	ew Classification (	Date   Reference		Claims	KWIC	Draw, Desc
				······································			***************************************
□ 139.	Document ID: U	JS 6495364 B2					
L26: Entr	y 139 of 189		File	: USPT	Dec	17,	2002

US-PAT-NO: 6495364

DOCUMENT-IDENTIFIER: US 6495364 B2

TITLE: Mx-1 conditionally immortalized cells

DATE-ISSUED: December 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Hammang; Joseph P. Barrington RI Messing; Albee Madison WI

US-CL-CURRENT: 435/320.1; 424/93.2, 435/325, 435/455, 514/44

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution

within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

2 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full Title Citation Front Review Classification Date Reference Claims KWIC Draw Des.

140. Document ID: US 6468794 B1

L26: Entry 140 of 189 File: USPT Oct 22, 2002

US-PAT-NO: 6468794

DOCUMENT-IDENTIFIER: US 6468794 B1

TITLE: Enriched central nervous system stem cell and progenitor cell populations, and methods for identifying, isolating and enriching for such populations

DATE-ISSUED: October 22, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Uchida; Nobuko Palo Alto CA
Buck; David W. Santa Clara CA
Weissman; Irving Redwood City CA

US-CL-CURRENT: 435/368; 435/343

### ABSTRACT:

Enriched neural stem and progenitor cell populations, and methods for identifying, isolating and enriching for neural stem cells using reagent that bind to cell surface markers, are provided.

13 Claims, 13 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 8

Full Title Citation Front	Review Classification C	ate Reference	Claims KMC Draw Des
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☐ 141. Document ID	: US 6399369 <sup>·</sup> B1		
L26: Entry 141 of 189		File: USPT	Jun 4, 2002

US-PAT-NO: 6399369

DOCUMENT-IDENTIFIER: US 6399369 B1

TITLE: Multipotent neural stem cell cDNA libraries

DATE-ISSUED: June 4, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Weiss; Samuel Calgary CA
Reynolds; Brent Saltspring CA

US-CL-CURRENT: 435/320.1; 435/368, 435/6, 435/91.1, 536/23.1, 536/23.5

# ABSTRACT:

cDNA libraries may be obtained from neural cell cultures produced by using growth factors to induce the proliferation of multipotent neural stem cells. The libraries may be obtained from both cultured normal and dysfunctional neural cells and from neural cell cultures at various stages of development. This information allows for the identification of the sequence of gene expression during neural development and can be used to reveal the effects of biological agents on gene expression in neural cells. Additionally, nucleic acid derived from dysfunctional tissue can be compared with that of normal tissue to identify genetic material which may be a cause of the dysfunction. This information could then be used in the design of therapies to treat the neurological disorder. A further use of the technology would be in the diagnosis of genetic disorders or for use in identifying neural cells at a particular stage in development.

5 Claims, 9 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full	Title	Citation Front Review	Classification	Date	Reference		Claims	KMC	Draw, Desj
***************************************	······					······································	 		
	142.	Document ID: US	6392118 B1						
L26:	Entry	142 of 189			File	: USPT	Мау	21,	2002

US-PAT-NO: 6392118

DOCUMENT-IDENTIFIER: US 6392118 B1

TITLE: Mx-1 conditionally immortalized cells

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Hammang; Joseph P. Barrington RI Messing; Albee Madison WI

US-CL-CURRENT: 800/14; 424/93.21, 435/320.1, 435/325, 435/455, 800/25

### ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically

manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

12 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full Title Citation Front Review Classification Date Reference Claims Review Classification Date Reference Claims Review Classification Date Reference Claims Review Claims Review Draw Description Claims Review Draw Dr

US-PAT-NO: 6361996

DOCUMENT-IDENTIFIER: US 6361996 B1

TITLE: Neuroepithelial stem cells and glial-restricted intermediate precursors

DATE-ISSUED: March 26, 2002

INVENTOR-INFORMATION:

NAME.

CITY

STATE ZIP CODE

COUNTRY

Rao; Mahendra S.

Salt Lake City

UT

Mayer-Proschel; Margot

Sandy

UT

US-CL-CURRENT: 435/353; 435/325

### ABSTRACT:

Multipotent neuroepithelial stem cells and lineage-restricted oligodendrocyte-astrocyte precursor cells are described. The neuroepithelial stem cells are capable of self-renewal and of differentiation into neurons, astrocytes, and oligodendrocytes. The oligodendrocyte-astrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into oligodendrocytes and astrocytes, but not neurons. Methods of generating, isolating, and culturing such neuroepithelial stem cells and oligodendrocyte-astrocyte precursor cells are also disclosed.

19 Claims, 2 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

Full	Title	Citation   Front   Review   Classification	Date Reference		Claims K	704C	Draw, Desi
	144.	Document ID: US 6326146 B1					
L26:	Entry	144 of 189	Fil	e: USPT	Dec	4,	2001

US-PAT-NO: 6326146

DOCUMENT-IDENTIFIER: US 6326146 B1

# \*\* See image for Certificate of Correction \*\*

TITLE: Method of determining multiple mRNAs in dying cells

DATE-ISSUED: December 4, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
O'Dell; Dianne M.	Drexel Hill	PA	19026	
Raghupathi; Ramesh	Devon	PA	19312	
McIntosh; Tracy Kahl	Wallingford	PA	19063	
Crino; Peter	Blenheim	NJ	08012	
Eberwine; James	Philadelphia	PA	19120	

US-CL-CURRENT: 435/6; 435/91.2

### ABSTRACT:

A method for determining expression levels of multiple mRNAs in single, dying cells from a selected tissue is provided. The method utilizes terminal deoxynucleotidyltransferase mediated biotin-dUTP nick end labeling to identify dying cells and measures multiple mRNA expression levels in single, isolated dying cells or portions thereof by amplified antisense RNA techniques.

2 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full   Title   Citation   Front   Review   Classification	Date Reference de la	Claims KMC Draw Desc
☐ 145. Document ID: US 6294346 B1	   File: USPT	Sep 25, 2001

US-PAT-NO: 6294346

DOCUMENT-IDENTIFIER: US 6294346 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Use of multipotent neural stem cells and their progeny for the screening of drugs and other biological agents

DATE-ISSUED: September 25, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Weiss; Samuel	Calgary			CA
Reynolds; Brent	Calgary			CA
Hammang; Joseph P.	Barrington	RI		
Baetge; E. Edward	Barrington	RI		

US-CL-CURRENT: 435/7.21; 435/368, 435/375, 435/377

### ABSTRACT:

A culture method for determining the effect of a biological agent on multipotent

neural stem cell progeny is provided. In the presence of growth factors, multipotent neural stem cells are induced to proliferate in culture. The multipotent neural stem cells may be obtained from normal neural tissue or from a donor afflicted with a disease such as Alzheimer's Disease, Parkinson's Disease or Down's Syndrome. At various stages in the differentiation process of the multipotent neural stem cell progeny, the effects of a biological agent, such as a virus, protein, peptide, amino acid, lipid, carbohydrate, nucleic acid or a drug or pro-drug on cell activity are determined. Additionally, a method of screening the effects of biological agents on a clonal population of neural cells is provided. The technology provides an efficient method for the generation of large numbers of pre- and post-natal neural cells under controlled, defined conditions. The disclosed cultures provide an optimal source of normal and diseased neural cells at various developmental stages, which can be screened for potential side effects in addition to testing the action and efficacy of different biological agents.

12 Claims, 9 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

US-PAT-NO: 6265175

DOCUMENT-IDENTIFIER: US 6265175 B1

TITLE: Method for production of neuroblasts

DATE-ISSUED: July 24, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA
Ray; Jasodhara San Diego CA

US-CL-CURRENT: 435/7.21; 435/29, 435/4, 435/7.1, 435/7.2

# ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblast and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

4 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Front Rev	riew Classification Date Refere	nce	Claims KMAC Drawn Desc

Jul 10, 2001 File: USPT L26: Entry 147 of 189

US-PAT-NO: 6258353

DOCUMENT-IDENTIFIER: US 6258353 B1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due

to neurodegenerative diseases

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Isacson; Ole

Cambridge

MΆ

Dinsmore; Jonathan

Brookline

MA

US-CL-CURRENT: 424/93.1; 424/130.1, 424/143.1, 424/809, 424/93.7, 435/325, 435/368

# ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

26 Claims, 62 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 24

Full Title Citation Front Review Classification Date Reference

Claims KWC Draw Des

☐ 148. Document ID: US 6245566 B1

L26: Entry 148 of 189

File: USPT

Jun 12, 2001

US-PAT-NO: 6245566

DOCUMENT-IDENTIFIER: US 6245566 B1

TITLE: Human embryonic germ cell line and methods of use

DATE-ISSUED: June 12, 2001

INVENTOR-INFORMATION:

NAME

CITY

ZIP CODE STATE

COUNTRY

Gearhart; John D.

Baltimore MD

Shamblott; Michael Joseph

Baltimore N

US-CL-CURRENT: 435/384; 435/366, 435/383

### ABSTRACT:

Primordial germ cells isolated from human embryonic tissue, such as from the gonadal ridges of human embryo, are disclosed. The primordial germ cells are cultured resulting in cells that resemble embryonic stem cells or embryonic germ cells in morphology and pluripotency. The cells are maintained several months in culture and can be genetically manipulated using transgenic technology to insert heterologous genetic material.

36 Claims, 10 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full	Title	Citation   Front   Review   Classification   Da			Claims KWAC	: Draw Desi
	149.	Document ID: US 6238922 B1				
L26:	Entry	149 of 189	File	: USPT	May 29	, 2001

US-PAT-NO: 6238922

DOCUMENT-IDENTIFIER: US 6238922 B1

TITLE: Use of collagenase in the preparation of neural stem cell cultures

DATE-ISSUED: May 29, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Uchida; Nobuko

Palo Alto

CA

US-CL-CURRENT: 435/380; 435/368, 435/378, 435/381

# ABSTRACT:

The invention provides a method for using collagenase to dissociate neural stem cells in neural stem cell cultures when passaging aggregated neural stem cells. The collagenase treatment results in an increased cell viability and an increased number of proliferated neural stem cells over time.

34 Claims, 1 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 1

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Fuli	Title	Citation Front Revie	ew Classification	Date	Reference		Claims	KWIC	Draw, D	<b>es</b> (
	<u>.</u>	<u>-</u>								
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п	150	Document ID: U	IS 6235527 R1							
	130.	Document in. C	0233321 101	L						
L26:	Entry	150 of 189			File	: USPT	Мау	, 22,	2001	

US-PAT-NO: 6235527

DOCUMENT-IDENTIFIER: US 6235527 B1

TITLE: Lineage restricted glial precursors from the central nervous system

DATE-ISSUED: May 22, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Rao; Mahendra S. Salt Lake City UT
Noble; Mark Sandy UT
Mayer-Proschel; Margot Sandy UT

US-CL-CURRENT: 435/325; 435/368, 435/378, 435/395, 435/402

### ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

5 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full	Title	Citation Front R	eview Classification	Date Reference		Claims	KAMC	Draw Desc
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L	151.	Document ID:	US 6214334 B1					0.001
L26:	Entry	151 of 189		File:	USPT	Apr	10,	2001

US-PAT-NO: 6214334

DOCUMENT-IDENTIFIER: US 6214334 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Compositions and methods for producing and using homogenous neuronal cell transplants to treat neurodegenerative disorders and brain and spinal cord injuries

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Lee; Virginia M. -Y. Philadelphia PA Trojanowski; John Q. Philadelphia PA

US-CL-CURRENT:  $\underline{424}/\underline{93.1}$ ;  $\underline{424}/\underline{93.7}$ ,  $\underline{435}/\underline{325}$ ,  $\underline{435}/\underline{347}$ ,  $\underline{435}/\underline{353}$ 

# ABSTRACT:

Methods of treating individuals suspected of suffering from diseases, conditions or disorders of the Central Nervous System which comprise implanting stable, homogeneous

post-mitotic human neurons into the individual's brain are disclosed. Methods of treating individuals suspected of suffering from injuries, diseases, conditions or disorders characterized by nerve damage which comprise implanting stable, homogeneous post-mitotic human neurons at or near a site of said nerve damage are also disclosed.

6 Claims, 21 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

Full	<u> </u>	Citation   Front				· · · · · · · · · · · · · · · · · · ·	KMC	Draw Desc
		Document II						***************************************
L26:	Entry	152 of 189		Fil	e: USPT	Fe.	b 6,	2001

US-PAT-NO: 6184035

DOCUMENT-IDENTIFIER: US 6184035 B1

TITLE: Methods for isolation and activation of, and control of differentiation from,

skeletal muscle stem or progenitor cells

DATE-ISSUED: February 6, 2001

INVENTOR-INFORMATION:

STATE COUNTRY NAME CITY ZIP CODE

South Pasadena Csete; Marie CA Doyle; John South Pasadena CA Wold; Barbara San Marino CA

US-CL-CURRENT: 435/377; 435/375

# ABSTRACT:

The present invention provides a method of isolating, maintaining, and/or enriching for stem or progenitor cells derived from diverse organ or tissue sources. The invention specifically teaches that these can be accomplished by the controlled use of subatmospheric oxygen culture, and that the precise oxygen level or levels must be determined empirically and/or by reference to physiologic levels within intact functioning organ or tissue. In particular, culturing skeletal muscle progenitor cells in less than 12% oxygen conditions or under 1% oxygen level.

16 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full	Title	Citation Front R	eview Classification	Date	Reference		Claims	KWAC	Draw, Desc
				······	·····		 		·····
	153.	Document ID:	US 6140116 A						
L26:	Entry	153 of 189			File:	USPT	Oct	31,	2000

US-PAT-NO: 6140116

DOCUMENT-IDENTIFIER: US 6140116 A

\*\* See image for Certificate of Correction \*\*

TITLE: Isolated and modified porcine cerebral cortical cells

DATE-ISSUED: October 31, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Dinsmore; Jonathan Brookline MA

US-CL-CURRENT: 435/325; 424/93.7, 435/374

#### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

27 Claims, 40 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 21

Full	Title	Citation Front Review Classification Date Reference Computer Communication Claims KWIC Draw, Desc
*************		
	154.	Document ID: US 6103530 A

File: USPT

US-PAT-NO: 6103530

DOCUMENT-IDENTIFIER: US 6103530 A

\*\* See image for Certificate of Correction \*\*

TITLE: Cultures of human CNS neural stem cells

DATE-ISSUED: August 15, 2000

L26: Entry 154 of 189

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Carpenter; Melissa Lincoln RI

US-CL-CURRENT: 435/405; 435/325, 435/368, 435/377, 435/384, 435/387, 435/389,

435/404, 435/406

ABSTRACT:

Aug 15, 2000

Isolation, characterization, proliferation, differentiation and transplantation of mammalian neural stem cells is disclosed.

2 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | South | South | South | Claims | KMC | Draw Desc

L26: Entry 155 of 189

File: USPT

Jun 6, 2000

US-PAT-NO: 6071889

DOCUMENT-IDENTIFIER: US 6071889 A

TITLE: In vivo genetic modification of growth factor-responsive neural precursor

cells

DATE-ISSUED: June 6, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Weiss; Samuel Alberta CA
Reynolds; Brent Alberta CA

Hammang; Joseph P. Barrington RI Baetge; E. Edward Barrington RI

US-CL-CURRENT: 514/44; 424/93.1, 424/93.2, 424/93.21, 435/440, 435/455

### ABSTRACT:

Methods for administering genetic material to dividing neural precursor cell populations in vivo are provided. The genetic material may comprise useful genes for neurotransmitters, growth factors, growth factor receptors, and the like. The genetic material is administered to the brain with one or more growth factors. The growth factors induce proliferation of neural precursor cells, thereby facilitating the incorporation of the genetic material into the cell progeny.

14 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full	Title	Citation Front Review		Reference		Claims	KMC	Drawi De	
·····		Document ID: US		***************************************	assaman assama	 amaaamaaaa			*****
L26:	Entry	156 of 189		Fil	e: USPT	Ap	r 4.	2000	

US-PAT-NO: 6045807

DOCUMENT-IDENTIFIER: US 6045807 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: April 4, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA Ray; Jasodhara San Diego CA

US-CL-CURRENT:  $\underline{424}/\underline{93.21}$ ;  $\underline{424}/\underline{93.7}$ ,  $\underline{435}/\underline{325}$ ,  $\underline{435}/\underline{366}$ ,  $\underline{435}/\underline{395}$ ,  $\underline{435}/\underline{402}$ ,  $\underline{435}/\underline{404}$ ,

536/23.1

#### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

9 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	Title	Citation   Front   Review   Classificatio	· <u> </u>				· ·	KWIC	Draw, Des
	157.	Document ID: US 6040180				·			
L26:	Entry	157 of 189		File:	USPT		Mar	21,	2000

US-PAT-NO: 6040180

DOCUMENT-IDENTIFIER: US 6040180 A

TITLE: In vitro generation of differentiated neurons from cultures of mammalian

multipotential CNS stem cells

DATE-ISSUED: March 21, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Johe; Karl K. Potomac MD

US-CL-CURRENT: 435/377; 435/325, 435/353, 435/368

# ABSTRACT:

The present invention reveals in vitro cultures of region-specific, terminally differentiated, mature neurons derived from cultures of mammalian multipotential CNS stem cells and an in vitro procedure by which the differentiated neurons may be generated. The procedure involves the culturing of multipotential CNS stem cells from a specific region in a chemically defined serum-free culture medium containing a growth factor; replacing the medium with growth factor-free medium; harvesting the stem cells by trypsinization; plating the stem cells at a density of between 100,000 to 250,000 cells per square centimeter; and culturing the stem cells in a glutamic acid-free chemically defined serum-free culture medium.

6 Claims, 80 Drawing figures Exemplary Claim Number: 1

Full Title Citation Front Review Classification Date Reference

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MC Draw, De

☐ 158. Document ID: US 6033906 A

L26: Entry 158 of 189

File: USPT

Mar 7, 2000

US-PAT-NO: 6033906

DOCUMENT-IDENTIFIER: US 6033906 A

TITLE: Methods for differentiating neural stem cells to glial cells using neuregulins

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

CA

US-CL-CURRENT: 435/325; 435/353, 435/368

### ABSTRACT:

Method for producing a population of mammalian glial cells comprising contacting at least one mammalian neural stem cell with a culture medium containing a neuregulin and detecting the differentiation of stem cell to a population of glial cells.

17 Claims, 60 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 22

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☐ 159. Document ID: US 6020197 A

L26: Entry 159 of 189

File: USPT

Feb 1, 2000

US-PAT-NO: 6020197

DOCUMENT-IDENTIFIER: US 6020197 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: February 1, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Gage; Fred H.

La Jolla

CA

Ray; Jasodhara

San Diego

CA

US-CL-CURRENT: 435/368; 435/325, 435/366, 435/395, 435/402, 435/404

ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

10 Claims, 17 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full Title Citation Front Review Classification Date Reference

Claims KMC Braw Desc

☐ 160. Document ID: US 6013521 A

L26: Entry 160 of 189

File: USPT

Jan 11, 2000

US-PAT-NO: 6013521

DOCUMENT-IDENTIFIER: US 6013521 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Gage; Fred H.

La Jolla

CA

Ray; Jasodhara

San Diego

CA

US-CL-CURRENT: 435/368; 435/325, 435/363, 435/366, 435/384, 435/387, 435/395, 435/402, 435/405, 435/406, 536/23.1

# ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

14 Claims, 34 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	Title	Citation	Front	Review	Classification	Date	Reference

Claims KWAC Draw Desi

☐ 161. Document ID: US 6001654 A

L26: Entry 161 of 189

File: USPT

Dec 14, 1999

US-PAT-NO: 6001654

DOCUMENT-IDENTIFIER: US 6001654 A

\*\* See image for Certificate of Correction \*\*

TITLE: Methods for differentiating neural stem cells to neurons or smooth muscle cells using TGT-.beta. super family growth factors

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA
Shah; Nirao M. New York NY

US-CL-CURRENT: 435/377; 435/325, 435/352, 435/353, 435/368, 435/375

# ABSTRACT:

Method for producing a population of mammalian neurons and/or smooth muscle cells comprising contacting at least one mammalian neural stem cell with a culture medium containing one or more growth factors from the TGF-.beta. super family and detecting the differentiation of stem cell to a population of neurons or smooth muscle cells.

22 Claims, 25 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 28

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Full Title Citation Front	Review Classification	Date	Reference		Claims	KWIC	Drawu Desc
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☐ 162. Document II	D: US 5981165 A						
L26: Entry 162 of 189			Fil	e: USPT	No	v 9,	1999

US-PAT-NO: 5981165

DOCUMENT-IDENTIFIER: US 5981165 A

TITLE: In vitro induction of dopaminergic cells

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Weiss; Samuel Alberta CA
Reynolds; Brent Alberta CA

US-CL-CURRENT: 435/4; 424/93.7, 435/325, 514/2, 530/399

# ABSTRACT:

A culture method for inducing the expression of tyrosine hydroxylase in neural cells is provided. Mammalian CNS neural cells are cultured in the presence of a fibroblast growth factor and at least one selected from a member of the transforming growth factor beta family, a feeder layer bed of cells, and cell conditioned medium. Cells cultured as provided above may be transplanted to provide dopaminergic cells to a patient. The cells may also be used in methods for drug screening.

41 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

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☐ 163. Document ID: US 5980885 A

L26: Entry 163 of 189

File: USPT

Nov 9, 1999

US-PAT-NO: 5980885

DOCUMENT-IDENTIFIER: US 5980885 A

TITLE: Growth factor-induced proliferation of neural precursor cells in vivo

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Weiss; Samuel Reynolds; Brent Alberta Alberta CA CA

US-CL-CURRENT: 424/93.21; 424/93.1, 424/93.2, 435/325, 435/360, 435/366, 435/368, 435/377, 435/383, 435/384, 435/440, 435/455, 435/456, 435/457, 514/2, 514/44

### ABSTRACT:

A method is described for inducing in vivo proliferation of precursor cells located in mammalian neural tissue by administering to the mammal a fibroblast growth factor and at least one additional growth factor selected from the group consisting of epidermal growth factor, transforming growth factor alpha, and amphiregulin. The method can be used to replace damaged or missing neurons and/or glia. Another method is described for transplanting multipotent neural stem cell progeny into a mammal. The method comprises the steps of administering growth factors to a mammal to induce in vivo proliferation of neural precursor cells, removing the precursor cell progeny from the mammal, culturing the removed cells in vitro in the presence of one or more growth factors that induces multipotent neural stem cell proliferation, and implanting the multipotent neural stem cell progeny into the mammal.

11 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

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laims KOMO Dravo Des-

☐ 164. Document ID: US 5968829 A

L26: Entry 164 of 189

File: USPT

Oct 19, 1999

US-PAT-NO: 5968829

DOCUMENT-IDENTIFIER: US 5968829 A

TITLE: Human CNS neural stem cells

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Carpenter; Melissa

Lincoln

US-CL-CURRENT: 435/467; 424/93.7, 435/368, 435/377

### ABSTRACT:

Isolation, characterization, proliferation, differentiation and transplantation of mammalian neural stem cells is disclosed.

RI

13 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Front Review Classification Date	Reference	Claims   KWIC   Draw. Des
☐ 165. Document ID: US 5958767 A L26: Entry 165 of 189	File: USPT	Sep 28, 1999
US-PAT-NO: 5958767 DOCUMENT-IDENTIFIER: US 5958767 A		
TITLE: Engraftable human neural stem cells		

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Snyder; Evan Y.

Jamaica Plain

MA

Wolfe; John H.

Philadelphia

PA

Kim; Seung U.

Vancouver

CA

US-CL-CURRENT: 435/368; 435/455

DATE-ISSUED: September 28, 1999

# ABSTRACT:

Stable clones of neural stem cells (NSCs) have been isolated from the human fetal telencephalon. In vitro, these self-renewing clones (affirmed by retroviral insertion site) can spontaneously give rise to all 3 fundamental neural cell types (neurons, oligodendrocytes, astrocytes). Following transplantation into germinal zones of the developing newborn mouse brain, they, like their rodent counterparts, can participate in aspects of normal development, including migration along well-established migratory pathways to disseminated CNS regions, differentiation into multiple developmentally- and regionally-appropriate cell types in response to microenvironmental cues, and non-disruptive, non-tumorigenic interspersion with host progenitors and their progeny. Readily genetically engineered prior to transplantation, human NSCs are capable of expressing foreign transgenes in vivo in these disseminated locations. Further supporting their potential for gene therapeutic applications, the secretory products from these NSCs can cross-correct a prototypical genetic metabolic defect in abnormal neurons and glia in vitro as effectively as do murine NSCs. Finally, human cells appear capable of replacing specific deficient neuronal populations in a mouse model of neurodegeneration and impaired development, much as murine NSCs could. Human NSCs may be propagated by a variety of means--both epigenetic (e.g., chronic mitogen exposure) and genetic (transduction of the propagating gene vmyc) -- that are comparably safe (vmyc is constitutively

downregulated by normal developmental mechanisms and environmental cues) and effective in yielding engraftable, migratory clones, suggesting that investigators may choose the propagation technique that best serves the demands of a particular research or clinical problem. All clones can be cryopreserved and transplanted into multiple hosts in multiple settings.

3 Claims, 43 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

Full	·:		ew Classification				• • • • • • • • • • • • • • • • • • •	KWIC	Draw. Desc
		Document ID: U		en e	***************************************		 ***************************************		
L26:	Entry	166 of 189			File	: USPT	Sep	28,	1999

US-PAT-NO: 5958688

DOCUMENT-IDENTIFIER: US 5958688 A

\*\* See image for Certificate of Correction \*\*

TITLE: Characterization of mRNA patterns in neurites and single cells for medical diagnosis and therapeutics

DATE-ISSUED: September 28, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Eberwine; James Philadelphia PA
Dichter; Marc Penn Valley PA
Miyashiro; Kevin Philadelphia PA

US-CL-CURRENT:  $\underline{435/6}$ ;  $\underline{435/91.21}$ ,  $\underline{435/91.51}$ ,  $\underline{536/23.5}$ ,  $\underline{536/24.31}$ ,  $\underline{536/24.33}$ 

# ABSTRACT:

A method of identifying neurite cDNA clones by determining and comparing mRNA expression in selected neurites is provided. cDNA clones identified by this method are also provided. In addition, methods of profiling mRNA expression and diagnosing and treating conditions associated with a pattern of mRNA expression by determining an mRNA expression profile in selected cells are provided.

4 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full	Title	Citation Front	Review	Classification	Date	Reference			Claims	KvelC	Draw Desi
		Document II						······································	•••••		
L26:	Entry	167 of 189				File:	USPT		Ju	27.	1999

US-PAT-NO: 5928947

DOCUMENT-IDENTIFIER: US 5928947 A

TITLE: Mammalian multipotent neural stem cells

DATE-ISSUED: July 27, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Newton MA

US-CL-CURRENT:  $\underline{435/455}$ ;  $\underline{424/93.7}$ ,  $\underline{435/325}$ ,  $\underline{435/440}$ ,  $\underline{435/69.1}$ 

### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

6 Claims, 20 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 22

Full	Title	Citation Front	Review	Classification	Date	Reference		Claims	KWAC	Draw, Desi
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	160	Document II	D. TIC S	966750 A						
ப	100.	Document II	<i>D.</i> US .	0000139 A						
L26:	Entry	168 of 189	ı			Fil	e: USPT	Fe	b 2,	1999

US-PAT-NO: 5866759

DOCUMENT-IDENTIFIER: US 5866759 A

TITLE: Transgenic mice expressing TSSV40 large T antigen

DATE-ISSUED: February 2, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Jat; Parmjit Singh London GB2

Kioussis; Dimitris London GB2

Noble; Mark David Berkhamstead GB2

US-CL-CURRENT: 800/18; 435/354

# ABSTRACT:

The provision of cell lines from virtually any cell type of the animal body is greatly facilitated by transgenic non-human eukaryotic animals of the invention in which at least some cells have (i) a differentiation inhibiting sequence

chromosomally incorporated under the control of a non-constitutive promotor and/or (ii) a differentiation inhibiting sequence which is itself conditionally active. Said genes are chromosomally incorporated under the control of a promotor such that expression of said sequence is normally held below an effective level, thus allowing normal cell development. However, cells taken from said animal may be prevented from completing differentiation to a non-dividing state in tissue culture by activating expression of said sequence.

8 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full	Title	Citation   Front   Review   Classification	Date Reference		Claims	KMC	Drawi Desi
	169.	Document ID: US 5858747 A					
L26:	Entry	169 of 189	File:	USPT	Jan	12,	1999

US-PAT-NO: 5858747

DOCUMENT-IDENTIFIER: US 5858747 A

TITLE: Control of cell growth in a bioartificial organ with extracellular matrix coated microcarriers

DATE-ISSUED: January 12, 1999

### INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto			CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			CH

US-CL-CURRENT: 435/182; 424/422, 424/93.21, 424/93.7, 435/176, 435/177, 435/178, 435/289.1, 435/377, 435/382, 435/395, 435/403

# ABSTRACT:

Methods and compositions are provided for controlling cell distribution within an implantable bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation—inhibiting compound or a differentiation—inducing compound or removing the cells from exposure to a proliferation—stimulating compound or a differentiation—inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the bioartificial organ with extracellular matrix molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. The bioartificial organ typically has a semipermeable membrane encapsulating a cell—containing core, and is preferably immunoisolatory. Cells can be grown on microcarriers and then loaded into the

bioartificial organ. The microcarriers may be coated with an extracellular matrix component such as collagen to cause decreased cell proliferation or increased cell differentiation. Microcarriers containing cells can be suspended in a proliferation inhibiting hydrogel matrix prior to encapsulation.

11 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full Title	Citation Front I	Review   Classification	Date   Reference		Claims	киис	Drawi Desi
·/····			***************************************		•	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
□ 170.	Document ID	: US 5853717 A		•			
L26: Entry	170 of 189		File	e: USPT	Dec	29,	1998

US-PAT-NO: 5853717

DOCUMENT-IDENTIFIER: US 5853717 A

TITLE: Methods and compositions of growth control for cells encapsulated within

bioartificial organs

DATE-ISSUED: December 29, 1998

### INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto			CA
Gentile; Frank T.	Warwick	RI ,		
Hammang; Joseph P.	Barrington	RI	•	
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			CA

US-CL-CURRENT: 424/93.21; 435/326, 435/372.2, 435/372.3, 435/382

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

14 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5 ☐ 171. Document ID: US 5851832 A

L26: Entry 171 of 189

File: USPT

Dec 22, 1998

CA

US-PAT-NO: 5851832

DOCUMENT-IDENTIFIER: US 5851832 A

TITLE: In vitro growth and proliferation of multipotent neural stem cells and their

progeny

DATE-ISSUED: December 22, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP

ITY STATE ZIP CODE COUNTRY

Weiss; Samuel Alberta

Reynolds; Brent Alberta CA

Hammang; Joseph P. Barrington RI Baetge; E. Edward Barrington RI

US-CL-CURRENT: <u>435/368</u>; <u>435/325</u>, <u>435/366</u>, <u>435/377</u>, <u>435/383</u>, <u>435/384</u>

ABSTRACT:

A method for the in vitro proliferation and differentiation of neural stem cells and stem cell progeny comprising the steps of (a) isolating the cells from a mammal, (b) exposing the cells to a culture medium containing a growth factor, (c) inducing the cells to proliferate, and (d) inducing the cells to differentiate is provided.

80 Claims, 9 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

2								
Full	Title	Citation	Front	Review	Classification	Date	Reference Claims KMC Draw Desc	

☐ 172. Document ID: US 5849553 A

L26: Entry 172 of 189

File: USPT

Dec 15, 1998

US-PAT-NO: 5849553

DOCUMENT-IDENTIFIER: US 5849553 A

TITLE: Mammalian multipotent neural stem cells

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA
Stemple; Derek L. Newton MA

US-CL-CURRENT: 435/467; 435/320.1, 435/325, 435/353, 435/368, 435/455, 435/462,

### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell, and immortalized cell lines which are capable of subsequent disimmortalization. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

25 Claims, 111 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 44

	•		
Full Title	Citation   Front   Review   Class	ification Date Reference	Claims KWC Draw. Desc
			,
□ 173.	Document ID: US 5843	431 A	
L26: Entr	y 173 of 189	File: USPT	Dec 1, 1998

US-PAT-NO: 5843431

DOCUMENT-IDENTIFIER: US 5843431 A

TITLE: Controlling proliferation of cells before and after encapsulation in a bioartificial organ by gene transformation

DATE-ISSUED: December 1, 1998

### INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto			CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			CH

US-CL-CURRENT: 424/93.21; 424/422, 424/93.7, 435/174, 435/178, 435/377, 435/382, 435/395, 435/467

# ABSTRACT:

Methods and compositions are provided for controlling cell distribution within an implantable bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a

growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the bioartificial organ with extracellular matrix molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. Cells can be transformed with a proliferationpromoting gene such as the oncogene, SV40, linked to a regulatable promoter such as the Mx1 promoter, the promotor is activated in vitro to express the gene to result in cell proliferation, and the promotor is inactivated before or after insertion of the cells in the bioartificial organ to inhibit expression of the gene to reduce or stop cell proliferation in vivo. The promoter can be reactivated in vivo to again express the gene to result in further cell proliferation. The gene may be a proliferationsuppressing gene such as p53 gene or RB gene, or a differentiation-inducing gene such as high mobility group chromosomal protein 14. Inhibiting gene expression in vitro causes cell proliferation, and inducing gene expression reduces or stops cell proliferation in vivo.

10 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	•	Citation Front Review Classification	· · ·		•	KMIC	Drawi Desc
		Document ID: US 5840576 A					
T/26:	Entry	174 of 189	File	: USPT	Nov	24.	1998

US-PAT-NO: 5840576

DOCUMENT-IDENTIFIER: US 5840576 A

TITLE: Methods and compositions of growth control for cells encapsulated within

bioartificial organs

DATE-ISSUED: November 24, 1998

# INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto		*	CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			CH

US-CL-CURRENT: 435/325; 435/375, 435/377, 435/400

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth

surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

4 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	Title	Citation   Front   Review   Classific	ation Date Ref	erence	Claims	KWIC	Drawt Desi
	175.	Document ID: US 58339	79 <b>A</b> `			***************************************	
L26:	Entry	175 of 189		File: USPT	Nov	10,	1998

US-PAT-NO: 5833979

DOCUMENT-IDENTIFIER: US 5833979 A

TITLE: Methods and compositions of growth control for cells encapsulated within

bioartificial organs

DATE-ISSUED: November 10, 1998

### INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto			CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			СН

US-CL-CURRENT: 424/93.21; 424/553, 424/556, 435/174, 435/352

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

2 Claims, 8 Drawing figures. Exemplary Claim Number: 1 Full Title Citation Front Review Classification Date Reference Claims KMC Draw Des

☐ 176. Document ID: US 5824489 A

L26: Entry 176 of 189

File: USPT

Oct 20, 1998

US-PAT-NO: 5824489

DOCUMENT-IDENTIFIER: US 5824489 A

TITLE: In vitro method for obtaining an isolated population of mammalian neural crest

stem cells

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J. Stemple; Derek L.

Altadena Pasadena

US-CL-CURRENT: 435/7.21; 435/325, 435/375, 435/377, 435/378, 435/395, 435/402

CA

### ABSTRACT:

The invention includes methods for the isolation and clonal propagation of mammalian neural stem cells. The methods employ a novel separation and culturing regimen and bioassays for establishing the generation of neural stem cell derivatives. These methods result in the production of non-transformed neural stem cells and their progeny. The invention demonstrates, at the clonal level, the self regeneration and asymmetrical division of mammalian neural stem cells for the first time in feeder cell-independent cultures. Lineage restriction is demonstrated within a developing clone and is shown to be sensitive to the local environment. Multipotent neural stem cells cultured on a mixed substrate of poly-D-lysine and fibronectin generate PNS neurons and glia, but on fibronectin alone the stem cells generate PNS glia but not neurons. The neurogenic potential of the stem cells, while not expressed, is maintained over time on fibronectin. The invention further includes transplantation assays which allow for the identification of mammalian neural stem cells from various tissues. It also includes methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals.

21 Claims, 48 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 16

Full Title Citation Front Review Classification Date Reference Claims KWC Draw Description 177. Document ID: US 5795790 A

File: USPT

US-PAT-NO: 5795790

L26: Entry 177 of 189

DOCUMENT-IDENTIFIER: US 5795790 A

Aug 18, 1998

TITLE: Method for controlling proliferation and differentiation of cells encapsulated within bioartificial organs

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto			CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		•
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			CH

US-CL-CURRENT: 435/382; 424/93.7, 435/177, 435/178, 435/180, 435/182

### ABSTRACT:

Methods and compositions are provided for controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the bioartificial organ with extracellular matrix molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. In a preferred treatment, cells are exposed to and then removed from exposure to a proliferation-stimulating and differentiation inhibiting compound prior to encapsulation of the cells in a semipermeable biocompatible jacket to form a bioartificial organ. Upon in vivo implantation of the bioartificial organ in a host, cellular proliferation is inhibited and cellular differentiation is promoted.

10 Claims, 8 Drawing figures Exemplary Claim Number: 6 Number of Drawing Sheets: 5

Full Title Citation Front F	Review Classification (	)ate Reference		Claims	KMC	Draw, Desc
					·····	
☐ 178. Document ID	: US 5792900 A					
L26: Entry 178 of 189		File:	USPT	Aug	11,	1998

US-PAT-NO: 5792900

DOCUMENT-IDENTIFIER: US 5792900 A

\*\* See image for Certificate of Correction \*\*

TITLE: Compositions and methods for producing and using homogenous neuronal cell transplants

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:

NAME

CITY

STATE ZIP CODE

COUNTRY

Lee; Virginia M.-Y.

Philadelphia

PA

Trojanowski; John Q.

Philadelphia

DΛ

US-CL-CURRENT: 800/12; 424/93.1, 424/93.2, 424/93.21, 424/93.7, 435/325, 435/368, 435/69.7, 435/70.1, 435/71.1, 800/9

### ABSTRACT:

The invention concerns populations of homogenous, post-mitotic human NT2N neurons that are useful for generating animal systems for study of neuron function. Also disclosed are methods of preparing animals that are useful for study of neurological function. In these methods, differentiated NT2N cells are stably implanted into host rodent animals.

11 Claims, 20 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	Title	Citation Front Review Classification	Date Reference		Claims Ki	MC	Drawi Desi
		Document ID: US 5776747 A					
T.26:	Entry	179 of 189	Fil	e: USPT	Jul	7. 1	998

US-PAT-NO: 5776747

DOCUMENT-IDENTIFIER: US 5776747 A

TITLE: Method for controlling the distribution of cells within a bioartificial organ using polycthylene oxide-poly (dimethylsiloxane) copolymer

DATE-ISSUED: July 7, 1998

# INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schinstine; Malcolm	Bensalem	PA		
Shoichet; Molly S.	Toronto .			CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RI		
Aebischer; Patrick	Lutry			CH

US-CL-CURRENT: 435/177; 435/180, 435/181, 435/182

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically

manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination. A particular embodiment is directed to derivatizing or adsorbing polyethylene oxide-poly (dimethylsiloxane) copolymer (PEO-PDMS) onto a surface within the bioartificial organ to inhibit cellular attachment.

2 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	Title	Citation Front Review Cl.	assification D	ate Reference			OMC	Draw, Desi
		Document ID: US 57			·	***************************************	***************************************	mmonomo de la composición dela composición de la composición de la composición dela composición dela composición dela composición de la co
L26:	Entry	180 of 189		File	: USPT	Jun	23,	1998

US-PAT-NO: 5770414

DOCUMENT-IDENTIFIER: US 5770414 A

TITLE: Regulatable retrovirus system for genetic modification of cells

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Gage; Fred H. La Jolla CA
Ray; Jasodhara San Diego CA

Hoshimaru; Minoru Shiga-ken JP

US-CL-CURRENT: 435/456; 435/320.1, 435/353, 435/357

### ABSTRACT:

A novel regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for immortalization of adult neuronal progenitor cells is provided. Regulation of a heterologous Producer cell lines which produce high titers of the recombinant retrovirus are also provided.

19 Claims, 18 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 8

Full	Title	Citation Front Review	Classification D	ate Reference		Claims KMC	Dravu Desi
		Document ID: US					<del>,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,</del>
L26:	Entry	181 of 189		File:	USPT	Jun 16,	1998.

US-PAT-NO: 5766948

DOCUMENT-IDENTIFIER: US 5766948 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: June 16, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA

Ray; Jasodhara San Diego CA

US-CL-CURRENT: 435/368; 435/325, 435/366, 435/395, 435/402, 435/404

#### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

7 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full	Title	Citation Front Review Classification Date Reference
	182.	Document ID: US 5753506 A

File: USPT

US-PAT-NO: 5753506

DOCUMENT-IDENTIFIER: US 5753506 A

TITLE: Isolation propagation and directed differentiation of stem cells from embryonic and adult central nervous system of mammals

DATE-ISSUED: May 19, 1998

L26: Entry 182 of 189

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Johe; Karl K. Potomac MD

US-CL-CURRENT: 435/377; 435/325, 435/366, 435/368

# ABSTRACT:

The present invention reveals an in vitro procedure by which a homogeneous population of multipotential precursor cells from mammalian embryonic neuroepithelium (CNS stem cells) can be expanded up to 10.sup.9 fold in culture while maintaining their multipotential capacity to differentiate into neurons, oligodendrocytes, and astrocytes. Chemically defined conditions are presented that enable a large number of neurons, up to 50% of the expanded cells, to be derived from the stem cells. In addition, four factors--PDGF, CNTF, LIF, and T3--have been identified which, individually, generate significantly higher proportions of neurons, astrocytes, or oligodendrocytes. These defined procedures permit a large-scale preparation of the

May 19, 1998

mammalian CNS stem cells, neurons, astrocytes, and oligodendrocytes under chemically defined conditions with efficiency and control. These cells should be an important tool for many cell- and gene-based therapies for neurological disorders.

16 Claims, 46 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 11

Full Title Citation Front Review Classification Date Reference Claims KMC Draw Des

File: USPT

US-PAT-NO: 5750376

DOCUMENT-IDENTIFIER: US 5750376 A

TITLE: In vitro growth and proliferation of genetically modified multipotent neural

stem cells and their progeny

L26: Entry 183 of 189

DATE-ISSUED: May 12, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Weiss; Samuel Alberta CA
Reynolds; Brent Alberta CA
Hammang; Joseph P. Barrington RI

Baetge; E. Edward Barrington RI

US-CL-CURRENT: 435/69.52; 435/325, 435/368, 435/377, 435/384, 435/392, 435/395, 435/455, 435/456, 435/458, 435/461, 435/69.1

### ABSTRACT:

A method for producing genetically modified neural cells comprises culturing cells derived from embryonic, juvenile, or adult mammalian neural tissue with one or more growth factors that induce multipotent neural stem cells to proliferate and produce multipotent neural stem cell progeny which include more daughter multipotent neural stem cells and undifferentiated progeny that are capable of differentiating into neurons, astrocytes, and oligodendrocytes. The proliferating neural cells can be transfected with exogenous DNA to produce genetically modified neural stem cell progeny. The genetic modification can be for the production of biologically useful proteins such as growth factor products, growth factor receptors, neurotransmitters, neurotransmitter receptors, neuropeptides and neurotransmitter synthesizing genes. The multipotent neural stem cell progeny can be continuously passaged and proliferation reinitiated in the presence of growth factors to result in an unlimited supply of neural cells for transplantation and other purposes. Culture conditions can be provided that induce the genetically modified multipotent neural stem cell progeny to differentiate into neurons, astrocytes, and oligodendrocytes in vitro.

40 Claims, 9 Drawing figures Exemplary Claim Number: 1,8,9 Number of Drawing Sheets: 3

Full Title Citation Front Review Classification Date Reference Claims	KWMC   Draw Desc
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May 12, 1998

# ☐ 184. Document ID: US 5728379 A

L26: Entry 184 of 189

File: USPT

Mar 17, 1998

US-PAT-NO: 5728379

DOCUMENT-IDENTIFIER: US 5728379 A

TITLE: Tumor- or cell-specific herpes simplex virus replication

DATE-ISSUED: March 17, 1998

INVENTOR-INFORMATION:

NAME

CITY STATE ZIP CODE

COUNTRY

Martuza; Robert L. Rabkin; Samuel D.

Chevy Chase

MD

Bethesda MD

Miyatake; Shin-ichi

Ohtsu

JP

US-CL-CURRENT: 424/93.2; 435/320.1, 435/456

### ABSTRACT:

A method for killing tumor cells in vivo entails providing replication competent herpes simplex virus vectors to tumor cells. A replication competent herpes simplex virus vector, with an essential herpes simplex virus gene which is driven by a tumor-specific or cell-specific promoter that specifically destroys tumor cells and is not neurovirulent. Also, a method for producing an animal model, by ablating a specific cell type in vivo, entails providing replication competent herpes simplex virus vectors to the animal. Such a vector, with an essential herpes simplex virus gene driven by a cell- or tissue-specific promoter, specifically destroys the target cell type. This method of viral-mediated gene therapy employs cell-specific viral replication, where viral replication and associated cytotoxicity are limited to a specific cell-type by the regulated expression of an essential immediate-early (IE) viral gene product.

13 Claims, 8 Drawing figures Exemplary Claim Number: 3 Number of Drawing Sheets: 8

Title Citation Front Review Classification Date Reference

laims KWiC Draw. De

☐ 185. Document ID: US 5693482 A

L26: Entry 185 of 189

File: USPT

Dec 2, 1997

US-PAT-NO: 5693482

DOCUMENT-IDENTIFIER: US 5693482 A

TITLE: Neural chest stem cell assay

DATE-ISSUED: December 2, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Stemple; Derek L.

Altadena Newton CA MA

US-CL-CURRENT: 435/29

ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

8 Claims, 62 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 23

Full	·	Citation   Front   Review	<u> </u>			<del></del>	<u> </u>
		Document ID: US				***************************************	
L26:	Entry	186 of 189		File:	USPT	Nov 18	, 1997

US-PAT-NO: 5688692

DOCUMENT-IDENTIFIER: US 5688692 A

\*\* See image for Certificate of Correction \*\*

TITLE: Transgenic mouse cells expressing ts SV40 large T

DATE-ISSUED: November 18, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Jat; Parmjit Singh London GB2
Kioussis; Dimitris London GB2
Noble; Mark David Berkhamstead GB2

US-CL-CURRENT: 435/354; 435/325, 435/377, 435/69.1

# ABSTRACT:

The provision of cell lines from virtually any cell type of the animal body is greatly facilitated by transgenic non-human eukaryotic animals of the invention in which at least some cells have (i) a differentiation inhibiting sequence chromosomally incorporated under the control of a non-constitutive promotor and/or (ii) a differentiation inhibiting sequence which is itself conditionally active. Said genes are chromosomally incorporated under the control of a promotor such that expression of said sequence is normally held below an effective level, thus allowing normal cell development. However, cells taken from said animal may be prevented from completing differentiation to a non-dividing state in tissue culture by activating

expression of said sequence.

18 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full Title Citation Front Review Classification Date Reference Communication Draws Description Claims KMC Draws Description

☐ 187. Document ID: US 5672499 A

L26: Entry 187 of 189

File: USPT

Sep 30, 1997

US-PAT-NO: 5672499

DOCUMENT-IDENTIFIER: US 5672499 A

TITLE: Immoralized neural crest stem cells and methods of making

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

CA

Stemple; Derek L.

Newton

MA

US-CL-CURRENT: 435/353; 435/320.1, 435/325, 435/368, 435/467, 435/69.1

### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

8 Claims, 62 Drawing figures Exemplary Claim Number: 1,2 Number of Drawing Sheets: 23

Full Title Citation Front Review Classification Date Reference

☐ 188. Document ID: US 5654183 A

L26: Entry 188 of 189

File: USPT

Aug 5, 1997

US-PAT-NO: 5654183

DOCUMENT-IDENTIFIER: US 5654183 A

TITLE: Genetically engineered mammalian neural crest stem cells

DATE-ISSUED: August 5, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Newton MA

US-CL-CURRENT: 435/456; 435/320.1, 435/325, 435/353, 435/368, 435/69.1

### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

17 Claims, 62 Drawing figures Exemplary Claim Number: 1,4 Number of Drawing Sheets: 23

Full		Citation Front Review Classification			Claims		Draw. Deso	
		Document ID: US 5589376 A			~~~~	***************************************	***************************************	
L26:	Entry	189 of 189	File	· USPT	Dec	31.	1996	

US-PAT-NO: 5589376

DOCUMENT-IDENTIFIER: US 5589376 A

TITLE: Mammalian neural crest stem cells

DATE-ISSUED: December 31, 1996

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Pasadena CA

US-CL-CURRENT: 435/325; 435/350, 435/351, 435/353, 435/363, 435/368

# ABSTRACT:

The invention includes methods for the isolation and clonal propagation of mammalian neural crest stem cells and isolated cellular compositions comprising the same. The methods employ a novel separation and culturing regimen and bioassays for establishing the generation of neural crest stem cell derivatives. These methods result in the production of non-transformed neural crest stem cells and their progeny. The invention demonstrates, at the clonal level, the self regeneration and asymmetrical division of mammalian neural crest stem cells for the first time in

feeder cell-independent cultures. Lineage restriction is demonstrated within a developing clone and is shown to be sensitive to the local environment. Neural crest stem cells cultured on a mixed substrate of poly-D-lysine and fibronectin generate PNS neurons and glia, but on fibronectin alone the stem cells generate PNS glia but not neurons. The neurogenic potential of the stem cells, while not expressed, is maintained over time on fibronectin. The invention further includes transplantation assays which allow for the identification of mammalian neural crest stem cells from various tissues. It also includes methods for transplanting mammalian neural crest stem cells and/or neural or glial progenitors into mammals.

10 Claims, 48 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 16

Full Title Citation Front Review Classification	n Date Reference	Claims KMC Draw Desi
Clear Generate Collection Prin	nt Fwd Refs Bkwd Refs	Generate OACS
Terms	Documents	
L22 AND L25	Documents	189

Display Format: - Change Format

Previous Page Next Page Go to Doc#

# Hit List

Clear Generate Collection Print Fwd Refs Bkwd Refs Generate OACS

# Search Results - Record(s) 1 through 48 of 48 returned.

☐ 1. Document ID: US 20040175823 A1

Using default format because multiple data bases are involved.

L31: Entry 1 of 48

File: PGPB

Sep 9, 2004

PGPUB-DOCUMENT-NUMBER: 20040175823

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040175823 A1

TITLE: Isolation of spore-like cells from tissues exposed to extreme conditions

PUBLICATION-DATE: September 9, 2004

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Vacanti, Charles A.

Lexington

MΑ

US

Vacanti, Martin P.

Westborough

MA

US

US-CL-CURRENT: 435/325

Full Title Citation	Fro Review	Classification Dat	e Reference	Sequences	Attachments	Claims	KMMC   Draw, Desi
	110	· ·					

# ☐ 2. Document ID: US 20030113869 A1

L31: Entry 2 of 48

File: PGPB

Jun 19, 2003

PGPUB-DOCUMENT-NUMBER: 20030113869

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030113869 A1

TITLE: Human FGF gene and gene expression products

PUBLICATION-DATE: June 19, 2003

INVENTOR-INFORMATION:

			*.	
NAME	CITY	STATE	COUNTRY	RULE-47
Cen, Hui	Alameda	CA	US	
Garcia, Pablo D.	San Francisco	CA	US	
Grieshammer, Uta	San Francisco	CA	US	
Kassam, Altaf	Alameda	CA	US	
Lee, Pauline P.	Contra Costa	CA	US	-
Pot, David	San Francisco	CA	US	
Gospodarowicz, Denis	Contra Costa	CA	US	
Martin, Kathleen	Alameda	CA	US	

US-CL-CURRENT: 435/69.4; 435/252.3, 435/254.1, 435/325, 530/399, 536/23.5

#### ABSTRACT:

This invention relates to human fibroblast growth factor (FGF 98), and to variants thereof and to polynucleotides encoding FGF 98. The invention also relates to diagnostic and therapeutic agents related to the polynucleotides and proteins, including probes and antibodies.

Full	Title Citation Fro Review Classification Date	Reference	Sequences	Attachments	Claims	KOMO	Drawa Desi
***************************************	~		***************************************	······		***************************************	
	3. Document ID: US 20020168763 A1						
L31:	Entry 3 of 48	File: F	GPB		Nov	14,	2002

PGPUB-DOCUMENT-NUMBER: 20020168763

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020168763 A1

TITLE: Isolated homozygous stem cells, differentiated cells derived therefrom, and materials and methods for making and using same

PUBLICATION-DATE: November 14, 2002

#### INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Yan, Wen Liang	Potomac	MD	US	
Huang, Steve Chien-Wen	Germantown	MD	US	
Nguyen, Minh-Thanh	Rockville	MD	US	
Lin, Hua (Helen)	Potomac	MD	US	
Lei, Jingqi	Gaithersburg	MD	US	
Khanna, Ruchi	Germantown	MD	US	

US-CL-CURRENT: 435/325; 435/350, 435/354, 435/366

## ABSTRACT:

The present invention discloses and describes pluripotent homozygous stem (HS) cells, and methods and materials for making same. The present invention also provides methods for differentiation of HS cells into progenitor (multipotent) cells or other desired cells, groups of cells or tissues. Further, the applications of the HS cells disclosed herein, include (but are not limited to) the diagnosis and treatment of various diseases (for example, genetic diseases, neurodegenerative diseases, endocrine-related disorders and cancer), traumatic injuries, cosmetic or therapeutic transplantation, gene therapy and cell replacement therapy.

Full Title Citation Fro Review Classification	Date Reference Sequences	Attachments Claims KWC Draw.	Des
			~~~~
·			
☐ 4. Document ID: US 20020151050 A	<b>\</b> 1		
L31: Entry 4 of 48	File: PGPB	Oct 17, 2002	>

PGPUB-DOCUMENT-NUMBER: 20020151050

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020151050 A1

TITLE: Isolation of spore-like cells from tissues exposed to extreme conditions

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

CITY STATE NAME COUNTRY RULE-47

Lexington Vacanti, Charles A. MA US Westborough MA US Vacanti, Martin P.

US-CL-CURRENT: 435/325

#### ABSTRACT:

Highly undifferentiated spore-like cells can be isolated from many different tissues and bodily fluids after those tissues and fluids have been exposed to extreme conditions. The spore-like cells can be used to treat a wide variety of disorders.

Full	Titl∈	: Citation	,, F	ro Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWC	Drawi Desc
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	5.	Docume	nt ID	): US 20	020045251	<b>A</b> 1						

File: PGPB Apr 18, 2002 L31: Entry 5 of 48

PGPUB-DOCUMENT-NUMBER: 20020045251

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020045251 A1

TITLE: COMMON NEURAL PROGENITOR FOR THE CNS AND PNS

PUBLICATION-DATE: April 18, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

RAO, MAHENDRA S. SALT LAKE CITY UT US MUJTABA, TAHMINA SANDY UTUS

US-CL-CURRENT: 435/325; 435/368, 435/373, 435/377, 435/383, 435/384, 435/387,

435/391, 435/395, 435/402

### ABSTRACT:

A method of generating neural crest stem cells involves inducing neuroepithelial stem cells to differentiate in vitro into neural crest stem cells. Differentiation can be induced by replating the cells on laminin, withdrawing mitogens, or adding dorsalizing agents to the growth medium. Derivatives of the peripheral nervous system can be generated by inducing the neural crest stem cells to differentiate in vitro.

Full Title Chaties	- Davison Classification	Data Reference Sequences	Attachments Claims KWIC Draw, Desi
Lan line citation	Fro Medievo Classification	pare   pererence   acditorioca	Litrogramente Cianne Mann Dezi

# ☐ 6. Document ID: US 20020009461 A1

L31: Entry 6 of 48 File: PGPB Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020009461

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020009461 A1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due

to neurodegenerative diseases

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

Isacson, Ole Cambridge MA US
Dinsmore, Jonathan Brookline MA US

US-CL-CURRENT: 424/193.1; 424/93.7, 435/325

#### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

Full Title Citation Fro Review Classifi	cation Date Reference Sequences Atta	ichments Claims KMC Draw. Desc
☐ 7. Document ID: US 2002000		· .
L31: Entry 7 of 48	File: PGPB	Jan 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020006660

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020006660 A1

TITLE: GENETICALLY-MODIFIED NEURAL PROGENITORS AND USES THEREOF

PUBLICATION-DATE: January 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE COUNTRY RULE-47

SABATE, OLIVIER PARIS FR

HORELLOU, PHILIPPE

PARIS

FR

BUC-CARON, MARIE-HELENE

PARIS

FR

MALLET, JACQUES

PARIS

FR

US-CL-CURRENT: 435/325; 514/44

# ABSTRACT:

The invention concerns human neural progenitor cells containing introduced genetic material encoding a product of interest, and their use for the treatment of neurodegenerative diseases.

Full Title Citation Fro Review Classifica	tion Date Reference Sequences Attac	chments Claims KWMC Draw Desc
☐ 8. Document ID: US 20010033	834 A1	
L31: Entry 8 of 48	File: PGPB	Oct 25, 2001

PGPUB-DOCUMENT-NUMBER: 20010033834

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010033834 A1

TITLE: Pleuripotent stem cells generated from adipose tissue-derived stromal cells

and uses thereof

PUBLICATION-DATE: October 25, 2001

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Wilkison, William O.

Bahama

NC NC US

Gimble, Jeffrey

Chapel Hill

; ι

US

US-CL-CURRENT: 424/93.7; 424/93.21, 435/325, 435/366, 435/368, 435/372

# ABSTRACT:

The invention is in the area of pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof. In particular, the invention includes isolated adipose tissue derived stromal cells that have been induced to express at least one phenotypic characteristic of a neuronal, astroglial, hematopoietic progenitor, or hepatic cell. The invention also includes an isolated adipocyte tissue-derived stromal cell that has been dedifferentiated such that there is an absence of adipocyte phenotypic markers.

Full Title Citation Fro Review Classification D	ate Reference Sequences Atta	achments Claims KWIC Draw. Desc
☐ 9. Document ID: US 20010029045 A	.1	
L31: Entry 9 of 48	File: PGPB	Oct 11, 2001

PGPUB-DOCUMENT-NUMBER: 20010029045

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010029045 A1

TITLE: Lineage restricted glial precursors from the central nervous system

PUBLICATION-DATE: October 11, 2001

INVENTOR-INFORMATION:

Mayer-Proschel, Margot

NAME CITY STATE COUNTRY RULE-47

Salt Lake City UT US Rao, Mahendra S. Brighton Noble, Mark NY US Pittsford US

US-CL-CURRENT: 435/325; 424/93.7

#### ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup. - fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

Full Title Citation	····· Fro	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw, Desc
							-			

# ☐ 10. Document ID: US 6787356 B1

L31: Entry 10 of 48 File: USPT Sep 7, 2004

US-PAT-NO: 6787356

DOCUMENT-IDENTIFIER: US 6787356 B1

TITLE: Cell expansion system for use in neural transplantation

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME CITY ZIP CODE COUNTRY STATE

Studer; Lorenz New York NY McKay; Ron D. Bethesda MD

US-CL-CURRENT: 435/377; 424/93.21, 435/325, 435/384, 514/44

# ABSTRACT:

The invention provides a method of culturing cells which includes a proliferating step in which the number of precursor cells is expanded and a differentiating step in which the expanded precursor cells develop into neuronal cells. The proliferating step includes the step of incubating the precursor cells in proliferating medium which includes basic fibroblast growth factor (bFGF). The differentiating step includes incubating the precursor cells in differentiation media in a manner effective to form a cellular aggregate that is not adhered to any surface of the incubation vessel. In a preferred embodiment, the cells are incubated in a roller tube. The differentiation media can also include at least one differentiating agent. The invention also provides a method for treating a neurological disorder, such as

Parkinson's disease, a method of introducing a gene product into a brain of a patient, an assay for neurologically active substances, and a cell culture.

23 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 8

Full | Title | Citation | Fro Review | Classification | Date | Reference | Claudian | Claims | Kivil | Drawl Desc

# ☐ 11. Document ID: US 6787355 B1

L31: Entry 11 of 48

File: USPT

Sep 7, 2004

US-PAT-NO: 6787355

DOCUMENT-IDENTIFIER: US 6787355 B1

TITLE: Multipotent neural stem cells from peripheral tissues and uses thereof

DATE-ISSUED: September 7, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Miller; Freda D. Montreal CA
Gloster; Andrew Saskatoon CA

Toma; Jean Montreal CA

US-CL-CURRENT: 435/377; 435/325, 435/375, 435/378, 435/383

# ABSTRACT:

This invention relates to multipotent neural stem cells, purified from the peripheral nervous system of mammals, capable of differentiating into neural and non-neural cell types. These stem cells provide an accessible source for autologous transplantation into CNS, PNS, and other damaged tissues.

8 Claims, 0 Drawing figures Exemplary Claim Number: 1

	on Date Reference	Claims KMC Draw Desc
☐ 12. Document ID: US 6767738 I		mmuuuuuun aali maasii mmaanaanaa sii saasii saa
L31: Entry 12 of 48	File: USPT	Jul 27, 2004

US-PAT-NO: 6767738

DOCUMENT-IDENTIFIER: US 6767738 B1

TITLE: Method of isolating adult mammalian CNS-derived progenitor stem cells using density gradient centrifugation

DATE-ISSUED: July 27, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA
Palmer; Theo San Carlos CA
Safar; Francis G. Irvine CA

Takahashi; Jun Kyoto JP
Takahashi; Masayo Kyoto JP

US-CL-CURRENT: 435/325; 435/366, 435/368, 435/378

#### ABSTRACT:

The present invention is directed to methods of repairing damaged or diseased, specialized or differentiated tissue in mature animals, particularly neuronal tissue such as retinas. In particular, the invention relates to transplantation of adult, hippocampus-derived progenitor cells into a selected neural tissue site of a recipient. These cells can functionally integrate into mature and immature neural tissue. The invention encompasses, in one aspect, repopulating a retina of a dystrophic animal with neurons, by injecting clonally derived, adult central nervous system derived stem cells (ACSC) derived from a healthy donor animal into an eye of the dystrophic recipient. Herein disclosed is the first successful and stable integration of clonally derived ACSC into same-species but different strain recipients (e. g., Fischer rat-derived adult hippocampal derived progenitor cells (AHPCs) into dystrophic RCS rats). Surprisingly, AHPCs were also found to integrate successfully into a xenogeneic recipient (e.g., rat AHPCs into the retina of dystropic rd-I mice).

13 Claims, 0 Drawing figures Exemplary Claim Number: 1

Full Title Citation Fro Review Classification	on Date Reference	Claims KMC Draw Desc
***************************************		
☐ 13. Document ID: US 6734015 I	31	
L31: Entry 13 of 48	File: USPT	May 11, 2004

US-PAT-NO: 6734015

DOCUMENT-IDENTIFIER: US 6734015 B1

TITLE: Isolation of lineage-restricted neuronal precursors

DATE-ISSUED: May 11, 2004

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Rao; Mahendra S. Salt Lake City UT Mayer-Proschel; Margot Sandy UT

US-CL-CURRENT: 435/368; 435/325

### ABSTRACT:

A self-renewing restricted stem cell population has been identified in developing (embryonic day 13.5) spinal cords that can differentiate into multiple neuronal phenotypes, but cannot differentiate into glial phenotypes. This neuronal-restricted precursor (NRP) expresses highly polysialated or embryonic neural cell adhesion

molecule (E-NCAM) and is morphologically distinct from neuroepithelial stem cells (NEP cells) and spinal glial progenitors derived from embryonic day 10.5 spinal cord. NRP cells self renew over multiple passages in the presence of fibroblast growth factor (FGF) and neurotrophin 3 (NT-3) and express a characteristic subset of neuronal epitopes. When cultured in the presence of RA and the absence of FGF, NRP cells differentiate into GABAergic, glutaminergic, and cholinergic immunoreactive neurons. NRP cells can also be generated from multipotent NEP cells cultured from embryonic day 10.5 neural tubes. Clonal analysis shows that E-NCAM immunoreactive NRP cells arise from an NEP progenitor cell that generates other restricted CNS precursors. The NEP-derived E-NCAM immunoreactive cells undergo self renewal in defined medium and differentiate into multiple neuronal phenotypes in mass and clonal culture. Thus, a direct lineal relationship exists between multipotential NEP cells and more restricted neuronal precursor cells present in vivo at embryonic day 13.5 in the spinal cord.

1 Claims, 1 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 1

Full Title Citation Fro Review Class	ification Date Reference	Claims KMC Draw, Desc
☐ 14. Document ID: US 66387	63 B1	
L31: Entry 14 of 48	File: USPT	Oct 28, 2003

US-PAT-NO: 6638763

DOCUMENT-IDENTIFIER: US 6638763 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Isolated mammalian neural stem cells, methods of making such cells

DATE-ISSUED: October 28, 2003

# INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Steindler; Dennis A.	Memphis	TN		
Laywell; Eric D.	Memphis	TN		
Kukekou; Valery G.	Memphis	TN		
Thomas; L. Brannon	Johnson City	TN		

US-CL-CURRENT: 435/368; 435/325, 435/377, 435/384

# ABSTRACT:

Using a novel culture approach, previously unknown populations of neural progenitor cells have been found within an adult mammalian brain. By limiting cell-cell contact, dissociated adult brain yields at least two types of cell aggregates. These aggregates or clones of stem/precursor cells can be generated from adult brain tissue with significantly long postmortem intervals. Both neurons and glia arise from stem/precursor cells of these cultures, and the cells can survive transplantation to the adult mammalian brain.

1 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 7

# ☐ 15. Document ID: US 6610540 B1

L31: Entry 15 of 48

File: USPT

Aug 26, 2003

US-PAT-NO: 6610540

DOCUMENT-IDENTIFIER: US 6610540 B1

TITLE: Low oxygen culturing of central nervous system progenitor cells

DATE-ISSUED: August 26, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Csete; Marie	Ann Arbor	MI		
Doyle; John	South Pasadena	CA		
Wold; Barbara J.	San Marino	CA		
McKay; Ron	Bethesda	MD		
Studer; Lorenz	New York	NY		

US-CL-CURRENT: 435/375; 435/325, 435/352, 435/368, 435/377, 435/4

## ABSTRACT:

The present invention relates to the growth of cells in culture under conditions that promote cell survival, proliferation, and/or cellular differentiation. The present inventors have found that proliferation was promoted and apoptosis reduced when cells were grown in lowered oxygen as compared to environmental oxygen conditions traditionally employed in cell culture techniques. Further, the inventors found that differentiation of precursor cells to specific fates also was enhanced in lowered oxygen where a much greater number and fraction of dopaminergic neurons were obtained when mesencephalic precursors were expanded and differentiated in lowered oxygen conditions. Thus at more physiological oxygen levels the proliferation and differentiation of CNS precursors is enhanced, and lowered oxygen is a useful adjunct for ex vivo generation of specific neuron types. Methods and compositions exploiting these findings are described.

11 Claims, 22 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 14

Full   Title   Citation   Fro Review   Classification		Claims KMC Draw Desi
☐ 16. Document ID: US 6610535 B	1	
L31: Entry 16 of 48	File: USPT	Aug 26, 2003

US-PAT-NO: 6610535

DOCUMENT-IDENTIFIER: US 6610535 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Progenitor cells and methods and uses related thereto

DATE-ISSUED: August 26, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Lu; Kuanghui Brookline MA
Pang; Kevin Canton MA
Rubin; Lee Wellesley MA

US-CL-CURRENT: 435/325; 435/363, 435/366, 435/372.2, 435/375, 435/377, 435/384, 435/387, 435/391, 435/392

#### ABSTRACT:

The present invention relates to a substantially pure population of viable pancreatic progenitor cells, and methods for isolating such cells. The present invention further concerns certain therapeutic uses for such progenitor cells, and their progeny.

16 Claims, 100 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 81

Full   Title   Citation   Fro Review   Classification   Date		
☐ 17. Document ID: US 6576464 B2 L31: Entry 17 of 48	File: USPT	Jun 10, 2003

US-PAT-NO: 6576464

DOCUMENT-IDENTIFIER: US 6576464 B2

TITLE: Methods for providing differentiated stem cells

DATE-ISSUED: June 10, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gold; Joseph D. San Francisco CA Lebkowski; Jane S. Portola Valley CA

US-CL-CURRENT: 435/325; 536/23.1, 536/23.4, 536/24.1, 536/25.5

# ABSTRACT:

This invention provides a system for producing differentiated cells from a stem cell population for use wherever a relatively homogenous cell population is desirable. The cells contain an effector gene under control of a transcriptional control element (such as the TERT promoter) that causes the gene to be expressed in relatively undifferentiated cells in the population. Expression of the effector gene results in depletion of undifferentiated cells, or expression of a marker that can be used to remove them later. Suitable effector sequences encode a toxin, a protein that induces apoptosis, a cell-surface antigen, or an enzyme (such as thymidine kinase) that converts a prodrug into a substance that is lethal to the cell. The differentiated cell populations produced according to this disclosure are suitable for use in tissue regeneration, and non-therapeutic applications such as drug screening.

30 Claims, 10 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 10

☐ 18. Document ID: US 6562619 B1

L31: Entry 18 of 48

File: USPT

May 13, 2003

US-PAT-NO: 6562619

DOCUMENT-IDENTIFIER: US 6562619 B1

TITLE: Differentiation of human embryonic germ cells

Full Title Citation Fro Review Classification Date Reference

DATE-ISSUED: May 13, 2003

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gearhart; John D. Baltimore MD Shamblott; Michael Joseph Baltimore MD

US-CL-CURRENT: 435/366; 424/93.21, 435/325

## ABSTRACT:

Primordial germ cells isolated from human embryonic tissue, such as from the gonadal ridges of human embryo, are disclosed. The primordial germ cells are cultured resulting in cells that resemble embryonic stem cells or embryonic germ cells in morphology and pluripotency. The cells are maintained several months in culture and can be genetically manipulated using transgenic technology to insert heterologous genetic material.

28 Claims, 10 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full Title Citation	Fro Review Classification	Date Reference	Claims KWIC Draw Desc

## ☐ 19. Document ID: US 6495364 B2

L31: Entry 19 of 48

File: USPT

Dec 17, 2002

US-PAT-NO: 6495364

DOCUMENT-IDENTIFIER: US 6495364 B2

TITLE: Mx-1 conditionally immortalized cells

DATE-ISSUED: December 17, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Hammang; Joseph P. Barrington RI

Messing; Albee

. . r ....

Madison

WI

US-CL-CURRENT: 435/320.1; 424/93.2, 435/325, 435/455, 514/44

#### ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

2 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full   Title   Citation   Fro Review	Classification Date Reference	Claims KMC Draw Desc
☐ 20. Document ID: US 6	5392118 B1 File: USPT	May 21, 2002

US-PAT-NO: 6392118

DOCUMENT-IDENTIFIER: US 6392118 B1

TITLE: Mx-1 conditionally immortalized cells

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Hammang; Joseph P. Barrington RI Messing; Albee Madison WI

US-CL-CURRENT: 800/14; 424/93.21, 435/320.1, 435/325, 435/455, 800/25

# ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

12 Claims, 8 Drawing figures Exemplary Claim Number: 1

Fro Review Classification Date Reference

☐ 21. Document ID: US 6361996 B1

L31: Entry 21 of 48

File: USPT

Mar 26, 2002

US-PAT-NO: 6361996

DOCUMENT-IDENTIFIER: US 6361996 B1

TITLE: Neuroepithelial stem cells and glial-restricted intermediate precursors

DATE-ISSUED: March 26, 2002

INVENTOR-INFORMATION:

NAME

Mayer-Proschel; Margot

CITY

Sandy

STATE ZIP CODE COUNTRY

Rao; Mahendra S.

Salt Lake City

UT

UT

US-CL-CURRENT: 435/353; 435/325

## ABSTRACT:

Multipotent neuroepithelial stem cells and lineage-restricted oligodendrocyteastrocyte precursor cells are described. The neuroepithelial stem cells are capable of self-renewal and of differentiation into neurons, astrocytes, and oligodendrocytes. The oligodendrocyte-astrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into oligodendrocytes and astrocytes, but not neurons. Methods of generating, isolating, and culturing such neuroepithelial stem cells and oligodendrocyte-astrocyte precursor cells are also disclosed.

19 Claims, 2 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

Full		eview   Classification	·		Claims KW	
	22. Document ID:				***************************************	······································
L31:	Entry 22 of 48		File:	USPT	Sep 4	4, 2001

US-PAT-NO: 6284539

DOCUMENT-IDENTIFIER: US 6284539 B1

TITLE: Method for generating dopaminergic cells derived from neural precursors

DATE-ISSUED: September 4, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

DC Bowen; David C. Washington

Johe; Karl K.

Potomac

MD

US-CL-CURRENT: 435/455; 424/93.21, 435/320.1, 435/325, 435/368, 514/44, 536/23.1,

536/23.5

#### ABSTRACT:

The present invention describes a novel method to direct a particular set of fate choice decisions by multipotential precursor cells from the central nervous system. Specifically we show that introducing the gene coding for the nuclear receptor, Nurrl, into central nervous system (CNS) stem cells causes cells to adopt a dopaminergic cell fate. One use of this technology would be to prepare in vitro neural populations enriched in dopaminergic cells for transplantation in Parkinson's Disease or other neurological disorders. Furthermore, the finding that Nurrl expression induces a dopaminergic phenotype suggests that introducing this gene into the brains of patients in which dopaminergic cells are degenerating or have been injured may promote the functional recovery of these neurons and thus the clinical recovery of the patient. Finally, the technology described in this application could be incorporated into a program of drug screening or gene discovery.

7 Claims, 23 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 23

Full Ti	tle   Citation	, Fro	Review	Classification	Date	Reference		Claims	KWAC	Draw Desi
□ 2:	B. Docum			258353 B						

File: USPT

Jul 10, 2001

US-PAT-NO: 6258353

L31: Entry 23 of 48

DOCUMENT-IDENTIFIER: US 6258353 B1

TITLE: Porcine neural cells and their use in treatment of neurological deficits due

to neurodegenerative diseases

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Isacson; Ole Cambridge MA
Dinsmore; Jonathan Brookline MA

US-CL-CURRENT:  $\underline{424/93.1}$ ;  $\underline{424/130.1}$ ,  $\underline{424/143.1}$ ,  $\underline{424/809}$ ,  $\underline{424/93.7}$ ,  $\underline{435/325}$ ,  $\underline{435/368}$ 

### ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is

essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

26 Claims, 62 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 24

Full Title Citation Fro Review Classification Date Reference Claims kWC Draw Description Date Reference Claims kWC Draw Description Date Reference Review Claims kWC Draw Description Date Review Claims kWC Draw Date Review Claims kWC Draw Description Date Review Claims kWC Dra

US-PAT-NO: 6235527

DOCUMENT-IDENTIFIER: US 6235527 B1

TITLE: Lineage restricted glial precursors from the central nervous system

DATE-ISSUED: May 22, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Rao; Mahendra S. Salt Lake City UT
Noble; Mark Sandy UT

Mayer-Proschel; Margot Sandy UT

US-CL-CURRENT: 435/325; 435/368, 435/378, 435/395, 435/402

## ABSTRACT:

A glial precursor cell population from mammalian central nervous system has been isolated. These A2B5.sup.+ E-NCAM.sup.- glial-restricted precursor (GRP) cells are capable of differentiating into oligodendrocytes, A2B5.sup.+ process-bearing astrocytes, and A2B5.sup.- fibroblast-like astrocytes, but not into neurons. GRP cells can be maintained by regeneration in culture. GRP cells differ from oligodendrocyte-type-2 astrocyte (O-2A) progenitor cells in growth factor requirements, morphology, and progeny. Methods of use of GRP cells are also disclosed.

5 Claims, 0 Drawing figures Exemplary Claim Number: 1

	Full	Title	Citation   Fro Review   Classification   Date   Reference   Classification   Claims   KMC	Draw, Desc
	~~~~			seeseenmannanna.
:		25.	Document ID: US 6214334 B1	

File: USPT

Apr 10, 2001

US-PAT-NO: 6214334

L31: Entry 25 of 48

DOCUMENT-IDENTIFIER: US 6214334 B1

# \*\* See image for Certificate of Correction \*\*

TITLE: Compositions and methods for producing and using homogenous neuronal cell transplants to treat neurodegenerative disorders and brain and spinal cord injuries

COUNTRY

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE

Lee; Virginia M. -Y. Philadelphia PA Trojanowski; John Q. Philadelphia PA

US-CL-CURRENT: 424/93.1; 424/93.7, 435/325, 435/347, 435/353

### ABSTRACT:

Methods of treating individuals suspected of suffering from diseases, conditions or disorders of the Central Nervous System which comprise implanting stable, homogeneous post-mitotic human neurons into the individual's brain are disclosed. Methods of treating individuals suspected of suffering from injuries, diseases, conditions or disorders characterized by nerve damage which comprise implanting stable, homogeneous post-mitotic human neurons at or near a site of said nerve damage are also disclosed.

6 Claims, 21 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 6

Full Title Citation Fro Review Classification Dat	te Reference	Claims KMMC Draw. Desi
☐ 26. Document ID: US 6140116 A		
L31: Entry 26 of 48	File: USPT	Oct 31, 2000

US-PAT-NO: 6140116

DOCUMENT-IDENTIFIER: US 6140116 A

\*\* See image for Certificate of Correction \*\*

TITLE: Isolated and modified porcine cerebral cortical cells

DATE-ISSUED: October 31, 2000

INVENTOR-INFORMATION:

NAME: CITY STATE ZIP CODE COUNTRY

Dinsmore; Jonathan Brookline MA

US-CL-CURRENT: 435/325; 424/93.7, 435/374

# ABSTRACT:

Porcine neural cells and methods for using the cells to treat neurological deficits due to neurodegeneration are described. The porcine neural cells are preferably embryonic mesencephalic, embryonic striatal cells, or embryonic cortical cells. The porcine neural cells can be modified to be suitable for transplantation into a xenogeneic subject, such as a human. For example, the porcine neural cells can be modified such that an antigen (e.g., an MHC class I antigen) on the cell surface which is capable of stimulating an immune response against the cell in a xenogeneic

http://westbrs:9000/bin/gate.exe?f=TOC&state=rfunta.33&ref=31&dbname=PGPB,USPT,U... 10/27/04

subject is altered (e.g., by contact with an anti-MHC class I antibody, or a fragment or derivative thereof) to inhibit rejection of the cell when introduced into the subject. In one embodiment, the porcine neural cells are obtained from a pig which is essentially free from organisms or substances which are capable of transmitting infection or disease to the recipient subject. The porcine neural cells of the present invention can be used to treat neurological deficits due to neurodegeneration in the brain of a xenogeneic subject (e.g., a human with epilepsy, head trauma, stroke, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, or Huntington's disease) by introducing the cells into the brain of the subject.

27 Claims, 40 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 21

Full Title Citation Fro Review Classification Date Reference

☐ 27. Document ID: US 6103530 A

L31: Entry 27 of 48

File: USPT

Aug 15, 2000

US-PAT-NO: 6103530

DOCUMENT-IDENTIFIER: US 6103530 A

\*\* See image for Certificate of Correction \*\*

TITLE: Cultures of human CNS neural stem cells

DATE-ISSUED: August 15, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Carpenter; Melissa

Lincoln

RT

US-CL-CURRENT: 435/405; 435/325, 435/368, 435/377, 435/384, 435/387, 435/389, 435/404, 435/406

## ABSTRACT:

Isolation, characterization, proliferation, differentiation and transplantation of mammalian neural stem cells is disclosed.

2 Claims, 7 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation Fro Review Classification Date Reference Claims KMC Draw. Des

☐ 28. Document ID: US 6045807 A

L31: Entry 28 of 48

File: USPT

Apr 4, 2000

US-PAT-NO: 6045807

DOCUMENT-IDENTIFIER: US 6045807 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: April 4, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA
Ray; Jasodhara San Diego CA

US-CL-CURRENT: 424/93.21; 424/93.7, 435/325, 435/366, 435/395, 435/402, 435/404,

536/23.1

### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

9 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full	Title Citation Fro Review Classification Date	Reference Cla	aims KMC Draw Desc
	29. Document ID: US 6040180 A		
L31:	Entry 29 of 48	File: USPT	Mar 21, 2000

US-PAT-NO: 6040180

DOCUMENT-IDENTIFIER: US 6040180 A

TITLE: In vitro generation of differentiated neurons from cultures of mammalian

multipotential CNS stem cells

DATE-ISSUED: March 21, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Johe; Karl K. Potomac MD

US-CL-CURRENT: 435/377; 435/325, 435/353, 435/368

## ABSTRACT:

The present invention reveals in vitro cultures of region-specific, terminally differentiated, mature neurons derived from cultures of mammalian multipotential CNS stem cells and an in vitro procedure by which the differentiated neurons may be generated. The procedure involves the culturing of multipotential CNS stem cells from a specific region in a chemically defined serum-free culture medium containing a growth factor; replacing the medium with growth factor-free medium; harvesting the stem cells by trypsinization; plating the stem cells at a density of between 100,000 to 250,000 cells per square centimeter; and culturing the stem cells in a glutamic acid-free chemically defined serum-free culture medium.

6 Claims, 80 Drawing figures Exemplary Claim Number: 1

Full Title Citation — Fro Review Classification Date Reference Claims KMC Draw. Desc

□ · 30. Document ID: US 6033906 A

L31: Entry 30 of 48

File: USPT

Mar 7, 2000

US-PAT-NO: 6033906

DOCUMENT-IDENTIFIER: US 6033906 A

TITLE: Methods for differentiating neural stem cells to glial cells using neuregulins

DATE-ISSUED: March 7, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

CA

US-CL-CURRENT: 435/325; 435/353, 435/368

## ABSTRACT:

Method for producing a population of mammalian glial cells comprising contacting at least one mammalian neural stem cell with a culture medium containing a neuregulin and detecting the differentiation of stem cell to a population of glial cells.

17 Claims, 60 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 22

Claims KMC Draw Desc	CI	Reference	Date	Classification	Fro Review	F	Citation	Title	Full
									-

☐ 31. Document ID: US 6020197 A

L31: Entry 31 of 48

File: USPT

Feb 1, 2000

US-PAT-NO: 6020197

DOCUMENT-IDENTIFIER: US 6020197 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: February 1, 2000

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Gage; Fred H.

La Jolla

CA

Ray; Jasodhara

San Diego

CA

US-CL-CURRENT:  $\underline{435}/\underline{368}$ ;  $\underline{435}/\underline{325}$ ,  $\underline{435}/\underline{366}$ ,  $\underline{435}/\underline{395}$ ,  $\underline{435}/\underline{402}$ ,  $\underline{435}/\underline{404}$ 

ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

10 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full Title Citation Fro Review Classificatio	n Date Reference	Claims   KWIC   Draw Desi
☐ 32. Document ID: US 6013521 A		
L31: Entry 32 of 48	File: USPT	Jan 11, 2000

US-PAT-NO: 6013521

DOCUMENT-IDENTIFIER: US 6013521 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Gage; Fred H. La Jolla CA Ray; Jasodhara San Diego CA

US-CL-CURRENT: 435/368; 435/325, 435/363, 435/366, 435/384, 435/387, 435/395, 435/402, 435/405, 435/406, 536/23.1

## ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

14 Claims, 34 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

	Date Reference	
☐ 33. Document ID: US 6001654 A		
L31: Entry 33 of 48	File: USPT	Dec 14, 1999

US-PAT-NO: 6001654

DOCUMENT-IDENTIFIER: US 6001654 A

\*\* See image for Certificate of Correction \*\*

TITLE: Methods for differentiating neural stem cells to neurons or smooth muscle cells using TGT-.beta. super family growth factors

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA
Shah; Nirao M. New York NY

US-CL-CURRENT: 435/377; 435/325, 435/352, 435/353, 435/368, 435/375

## ABSTRACT:

Method for producing a population of mammalian neurons and/or smooth muscle cells comprising contacting at least one mammalian neural stem cell with a culture medium containing one or more growth factors from the TGF-.beta. super family and detecting the differentiation of stem cell to a population of neurons or smooth muscle cells.

22 Claims, 25 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 28

Fuil		Classification Date Reference	
	34. Document ID: US 598	81165 A	
L31: H	Entry 34 of 48	File: USPT	Nov 9, 1999

US-PAT-NO: 5981165

DOCUMENT-IDENTIFIER: US 5981165 A

TITLE: In vitro induction of dopaminergic cells

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Weiss; Samuel Alberta CA
Reynolds; Brent Alberta CA

US-CL-CURRENT: 435/4; 424/93.7, 435/325, 514/2, 530/399

# ABSTRACT:

A culture method for inducing the expression of tyrosine hydroxylase in neural cells is provided. Mammalian CNS neural cells are cultured in the presence of a fibroblast growth factor and at least one selected from a member of the transforming growth factor beta family, a feeder layer bed of cells, and cell conditioned medium. Cells cultured as provided above may be transplanted to provide dopaminergic cells to a patient. The cells may also be used in methods for drug screening.

41 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2

# ☐ 35. Document ID: US 5980885 A

L31: Entry 35 of 48

File: USPT

Nov 9, 1999

US-PAT-NO: 5980885

DOCUMENT-IDENTIFIER: US 5980885 A

TITLE: Growth factor-induced proliferation of neural precursor cells in vivo

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Weiss; Samuel Reynolds; Brent Alberta -Alberta

CA

CA

US-CL-CURRENT:  $\underline{424/93.21}$ ;  $\underline{424/93.1}$ ,  $\underline{424/93.2}$ ,  $\underline{435/325}$ ,  $\underline{435/360}$ ,  $\underline{435/366}$ ,  $\underline{435/368}$ , 435/377, 435/383, 435/384, 435/440, 435/455, 435/456, 435/457, 514/2, 514/44

# ABSTRACT:

A method is described for inducing in vivo proliferation of precursor cells located in mammalian neural tissue by administering to the mammal a fibroblast growth factor and at least one additional growth factor selected from the group consisting of epidermal growth factor, transforming growth factor alpha, and amphiregulin. The method can be used to replace damaged or missing neurons and/or glia. Another method is described for transplanting multipotent neural stem cell progeny into a mammal. The method comprises the steps of administering growth factors to a mammal to induce in vivo proliferation of neural precursor cells, removing the precursor cell progeny from the mammal, culturing the removed cells in vitro in the presence of one or more growth factors that induces multipotent neural stem cell proliferation, and implanting the multipotent neural stem cell progeny into the mammal.

11 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full Title Citation Fro Review Classification	Date Reference	Claims KWIC Draw Des
☐ 36. Document ID: US 5928947 A		
L31: Entry 36 of 48	File: USPT	Jul 27, 1999

US-PAT-NO: 5928947

DOCUMENT-IDENTIFIER: US 5928947 A

TITLE: Mammalian multipotent neural stem cells

DATE-ISSUED: July 27, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Newton MA

US-CL-CURRENT: <u>435/455</u>; <u>424/93.7</u>, <u>435/325</u>, <u>435/440</u>, <u>435/69.1</u>

## ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

6 Claims, 20 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 22

Full   Title   Citation   Fro Review   Classification	Date Reference	Claims   KMC   Draw Desc
☐ 37. Document ID: US 5851832 A L31: Entry 37 of 48		Dec 22, 1998

US-PAT-NO: 5851832

DOCUMENT-IDENTIFIER: US 5851832 A

TITLE: In vitro growth and proliferation of multipotent neural stem cells and their progeny

progerry

DATE-ISSUED: December 22, 1998

# INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Weiss; Samuel Alberta CA CA Reynolds; Brent Alberta Hammang; Joseph P. , Barrington RIBaetge; E. Edward Barrington

US-CL-CURRENT: 435/368; 435/325, 435/366, 435/377, 435/383, 435/384

# ABSTRACT:

A method for the in vitro proliferation and differentiation of neural stem cells and stem cell progeny comprising the steps of (a) isolating the cells from a mammal, (b) exposing the cells to a culture medium containing a growth factor, (c) inducing the cells to proliferate, and (d) inducing the cells to differentiate is provided.

80 Claims, 9 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full Title Citation Fro Review Classification Date Reference

Claims KWC Draw Des

# ☐ 38. Document ID: US 5849553 A

L31: Entry 38 of 48

File: USPT

Dec 15, 1998

US-PAT-NO: 5849553

DOCUMENT-IDENTIFIER: US 5849553 A

TITLE: Mammalian multipotent neural stem cells

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Anderson; David J.

Altadena

dena CA

*-*A

Stemple; Derek L. Newton

MA

US-CL-CURRENT: 435/467; 435/320.1, 435/325, 435/353, 435/368, 435/455, 435/462,

435/69.1

## ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell, and immortalized cell lines which are capable of subsequent disimmortalization. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

25 Claims, 111 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 44

Full | Title | Citation | Fro Review | Classification | Date | Reference | Section | Claims | KiMC | Drawi Desi

☐ 39. Document ID: US 5840576 A

L31: Entry 39 of 48

File: USPT

Nov 24, 1998

US-PAT-NO: 5840576

DOCUMENT-IDENTIFIER: US 5840576 A

TITLE: Methods and compositions of growth control for cells encapsulated within bioartificial organs

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY -
Schinstine; Malcolm	Ben Salem	PA		
Shoichet; Molly S.	Toronto			CA
Gentile; Frank T.	Warwick	RI		
Hammang; Joseph P.	Barrington	RI		
Holland; Laura M.	Horsham	PA		
Cain; Brian M.	Everett	MA		•
Doherty; Edward J.	Mansfield	MA		
Winn; Shelley R.	Smithfield	RÍ		
Aebischer; Patrick	Lutry			СН

US-CL-CURRENT: 435/325; 435/375, 435/377, 435/400

#### ABSTRACT:

This invention relates to methods and compositions of controlling cell distribution within a bioartificial organ by exposing the cells to a treatment that inhibits cell proliferation, promotes cell differentiation, or affects cell attachment to a growth surface within the bioartificial organ. Such treatments include (1) genetically manipulating cells, (2) exposing the cells to a proliferation-inhibiting compound or a differentiation-inducing compound or removing the cells from exposure to a proliferation-stimulating compound or a differentiation-inhibiting compound; exposing the cells to irradiation, and (3) modifying a growth surface of the BAO with ECM molecules, molecules affecting cell proliferation or adhesion, or an inert scaffold, or a combination thereof. These treatments may be used in combination.

4 Claims, 8 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

Full   Title   Citation   Fro   Review   Classification	Date Reference	Claims KMC Draw, Desc
☐ 40. Document ID: US 5824489 A		
1.31: Entry 40 of 48	File: HSPT	Oct 20 1998

US-PAT-NO: 5824489

DOCUMENT-IDENTIFIER: US 5824489 A

TITLE: In vitro method for obtaining an isolated population of mammalian neural crest stem cells

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY
Anderson; David J. Altadena CA
Stemple; Derek L. Pasadena CA

US-CL-CURRENT: 435/7.21; 435/325, 435/375, 435/377, 435/378, 435/395, 435/402

### ABSTRACT:

The invention includes methods for the isolation and clonal propagation of mammalian neural stem cells. The methods employ a novel separation and culturing regimen and bioassays for establishing the generation of neural stem cell derivatives. These methods result in the production of non-transformed neural stem cells and their progeny. The invention demonstrates, at the clonal level, the self regeneration and asymmetrical division of mammalian neural stem cells for the first time in feeder cell-independent cultures. Lineage restriction is demonstrated within a developing clone and is shown to be sensitive to the local environment. Multipotent neural stem cells cultured on a mixed substrate of poly-D-lysine and fibronectin generate PNS neurons and glia, but on fibronectin alone the stem cells generate PNS glia but not neurons. The neurogenic potential of the stem cells, while not expressed, is maintained over time on fibronectin. The invention further includes transplantation assays which allow for the identification of mammalian neural stem cells from various tissues. It also includes methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals.

21 Claims, 48 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 16

Full   Title   Citation   Fro Review   Classification   C	Date Reference (1999)	
☐ 41. Document ID: US 5792900 A	<b>.</b>	- 44 1000
L31: Entry 41 of 48	File: USPT	Aug 11, 1998

US-PAT-NO: 5792900

DOCUMENT-IDENTIFIER: US 5792900 A

\*\* See image for <u>Certificate of Correction</u> \*\*

TITLE: Compositions and methods for producing and using homogenous neuronal cell transplants

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Lee; Virginia M.-Y. Philadelphia PA
Trojanowski; John Q. Philadelphia PA

US-CL-CURRENT: 800/12; 424/93.1, 424/93.2, 424/93.21, 424/93.7, 435/325, 435/368, 435/69.7, 435/70.1, 435/71.1, 800/9

## ABSTRACT:

The invention concerns populations of homogenous, post-mitotic human NT2N neurons that are useful for generating animal systems for study of neuron function. Also disclosed are methods of preparing animals that are useful for study of neurological function. In these methods, differentiated NT2N cells are stably implanted into host rodent animals.

11 Claims, 20 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 5

# ☐ 42. Document ID: US 5766948 A

L31: Entry 42 of 48

File: USPT

Jun 16, 1998

US-PAT-NO: 5766948

DOCUMENT-IDENTIFIER: US 5766948 A

TITLE: Method for production of neuroblasts

DATE-ISSUED: June 16, 1998

INVENTOR-INFORMATION:

NAME

CTTY

STATE

ZIP CODE

COUNTRY

Gage; Fred H.

La Jolla

CA

Ray; Jasodhara

San Diego

CA

US-CL-CURRENT: 435/368; 435/325, 435/366, 435/395, 435/402, 435/404

#### ABSTRACT:

A method for producing a neuroblast and a cellular composition comprising an enriched population of neuroblast cells is provided. Also disclosed are methods for identifying compositions which affect neuroblasts and for treating a subject with a neuronal disorder, and a culture system for the production and maintenance of neuroblasts.

7 Claims, 17 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 4

Full Title Citation	Fro Review Classification Date	Reference Claims	KMMC   Draw Desi
		•	

# ☐ 43. Document ID: US 5753506 A

L31: Entry 43 of 48

File: USPT

May 19, 1998

US-PAT-NO: 5753506

DOCUMENT-IDENTIFIER: US 5753506 A

TITLE: Isolation propagation and directed differentiation of stem cells from embryonic and adult central nervous system of mammals

DATE-ISSUED: May 19, 1998

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Johe; Karl K.

Potomac

MD

US-CL-CURRENT: 435/377; 435/325, 435/366, 435/368

### ABSTRACT:

The present invention reveals an in vitro procedure by which a homogeneous population of multipotential precursor cells from mammalian embryonic neuroepithelium (CNS stem cells) can be expanded up to 10.sup.9 fold in culture while maintaining their multipotential capacity to differentiate into neurons, oligodendrocytes, and astrocytes. Chemically defined conditions are presented that enable a large number of neurons, up to 50% of the expanded cells, to be derived from the stem cells. In addition, four factors—PDGF, CNTF, LIF, and T3—have been identified which, individually, generate significantly higher proportions of neurons, astrocytes, or oligodendrocytes. These defined procedures permit a large—scale preparation of the mammalian CNS stem cells, neurons, astrocytes, and oligodendrocytes under chemically defined conditions with efficiency and control. These cells should be an important tool for many cell— and gene—based therapies for neurological disorders.

16 Claims, 46 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 11

Full Title Citation Fro Review Classification Dar	te Reference	Claims KWMC Draw, Des
☐ 44. Document ID: US 5750376 A L31: Entry 44 of 48	File: USPT	May 12, 1998

US-PAT-NO: 5750376

DOCUMENT-IDENTIFIER: US 5750376 A

TITLE: In vitro growth and proliferation of genetically modified multipotent neural stem cells and their progeny

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DATE-ISSUED: May 12, 1998

## INVENTOR-INFORMATION:

COUNTRY CITY STATE ZIP CODE NAME. CA Alberta Weiss; Samuel CA Alberta Reynolds; Brent RΙ Barrington Hammang; Joseph P. RΙ Barrington Baetge; E. Edward

US-CL-CURRENT: 435/69.52; 435/325, 435/368, 435/377, 435/384, 435/392, 435/395, 435/455, 435/456, 435/458, 435/461, 435/69.1

# ABSTRACT:

A method for producing genetically modified neural cells comprises culturing cells derived from embryonic, juvenile, or adult mammalian neural tissue with one or more growth factors that induce multipotent neural stem cells to proliferate and produce multipotent neural stem cell progeny which include more daughter multipotent neural stem cells and undifferentiated progeny that are capable of differentiating into neurons, astrocytes, and oligodendrocytes. The proliferating neural cells can be transfected with exogenous DNA to produce genetically modified neural stem cell progeny. The genetic modification can be for the production of biologically useful proteins such as growth factor products, growth factor receptors, neurotransmitters, neurotransmitter receptors, neuropeptides and neurotransmitter synthesizing genes. The multipotent neural stem cell progeny can be continuously passaged and proliferation reinitiated in the presence of growth factors to result in an unlimited

supply of neural cells for transplantation and other purposes. Culture conditions can be provided that induce the genetically modified multipotent neural stem cell progeny to differentiate into neurons, astrocytes, and oligodendrocytes in vitro.

40 Claims, 9 Drawing figures Exemplary Claim Number: 1,8,9 Number of Drawing Sheets: 3

Full   Title   Citation   Fro Review   Classification   D			KMC   Draw Desi
☐ 45. Document ID: US 5688692 A			
L31: Entry 45 of 48	File: USPT	Nov	18, 1997

US-PAT-NO: 5688692

DOCUMENT-IDENTIFIER: US 5688692 A

\*\* See image for Certificate of Correction \*\*

TITLE: Transgenic mouse cells expressing ts SV40 large T

DATE-ISSUED: November 18, 1997

INVENTOR-INFORMATION:

CTTY STATE ZIP CODE COUNTRY NAME Jat; Parmjit Singh London GB2 Kioussis; Dimitris London GB2 Noble; Mark David GB2 Berkhamstead

US-CL-CURRENT: 435/354; 435/325, 435/377, 435/69.1

## ABSTRACT:

The provision of cell lines from virtually any cell type of the animal body is greatly facilitated by transgenic non-human eukaryotic animals of the invention in which at least some cells have (i) a differentiation inhibiting sequence chromosomally incorporated under the control of a non-constitutive promotor and/or (ii) a differentiation inhibiting sequence which is itself conditionally active. Said genes are chromosomally incorporated under the control of a promotor such that expression of said sequence is normally held below an effective level, thus allowing normal cell development. However, cells taken from said animal may be prevented from completing differentiation to a non-dividing state in tissue culture by activating expression of said sequence.

18 Claims, 3 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 3

Full Title Citation Fro Review Classific	ation Date Reference	Claims KMC Draw, Des)
☐ 46. Document ID: US 5672499	9 A	
L31: Entry 46 of 48	File: USPT	Sep 30, 1997

US-PAT-NO: 5672499

DOCUMENT-IDENTIFIER: US 5672499 A

TITLE: Immoralized neural crest stem cells and methods of making

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Newton MA

US-CL-CURRENT: 435/353; 435/320.1, 435/325, 435/368, 435/467, 435/69.1

#### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

8 Claims, 62 Drawing figures Exemplary Claim Number: 1,2 Number of Drawing Sheets: 23

Full	Title Citation Fro Review Classification Date	Reference	laims KMMC Draw Desc
	47. Document ID: US 5654183 A		
L31:	Entry 47 of 48	File: USPT	Aug 5, 1997

US-PAT-NO: 5654183

DOCUMENT-IDENTIFIER: US 5654183 A

TITLE: Genetically engineered mammalian neural crest stem cells

DATE-ISSUED: August 5, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY

Anderson; David J. Altadena CA Stemple; Derek L. Newton MA

US-CL-CURRENT: 435/456; 435/320.1, 435/325, 435/353, 435/368, 435/69.1

### ABSTRACT:

The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level

the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

17 Claims, 62 Drawing figures Exemplary Claim Number: 1,4 Number of Drawing Sheets: 23

Full   Title   Citation   Fro Review   Classification		
☐ 48. Document ID: US 5589376 A		•
1.31: Entry 48 of 48	File: USPT	Dec 31, 1996

US-PAT-NO: 5589376

L31: Entry 48 of 48

DOCUMENT-IDENTIFIER: US 5589376 A

TITLE: Mammalian neural crest stem cells

DATE-ISSUED: December 31, 1996

INVENTOR-INFORMATION:

ZIP CODE COUNTRY STATE CITY NAME

Altadena CA Anderson; David J. Pasadena CA Stemple; Derek L.

US-CL-CURRENT: 435/325; 435/350, 435/351, 435/353, 435/363, 435/368

### ABSTRACT:

The invention includes methods for the isolation and clonal propagation of mammalian neural crest stem cells and isolated cellular compositions comprising the same. The methods employ a novel separation and culturing regimen and bioassays for establishing the generation of neural crest stem cell derivatives. These methods result in the production of non-transformed neural crest stem cells and their progeny. The invention demonstrates, at the clonal level, the self regeneration and asymmetrical division of mammalian neural crest stem cells for the first time in feeder cell-independent cultures. Lineage restriction is demonstrated within a developing clone and is shown to be sensitive to the local environment. Neural crest stem cells cultured on a mixed substrate of poly-D-lysine and fibronectin generate PNS neurons and glia, but on fibronectin alone the stem cells generate PNS glia but not neurons. The neurogenic potential of the stem cells, while not expressed, is maintained over time on fibronectin. The invention further includes transplantation assays which allow for the identification of mammalian neural crest stem cells from various tissues. It also includes methods for transplanting mammalian neural crest stem cells and/or neural or glial progenitors into mammals.

10 Claims, 48 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 16

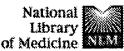
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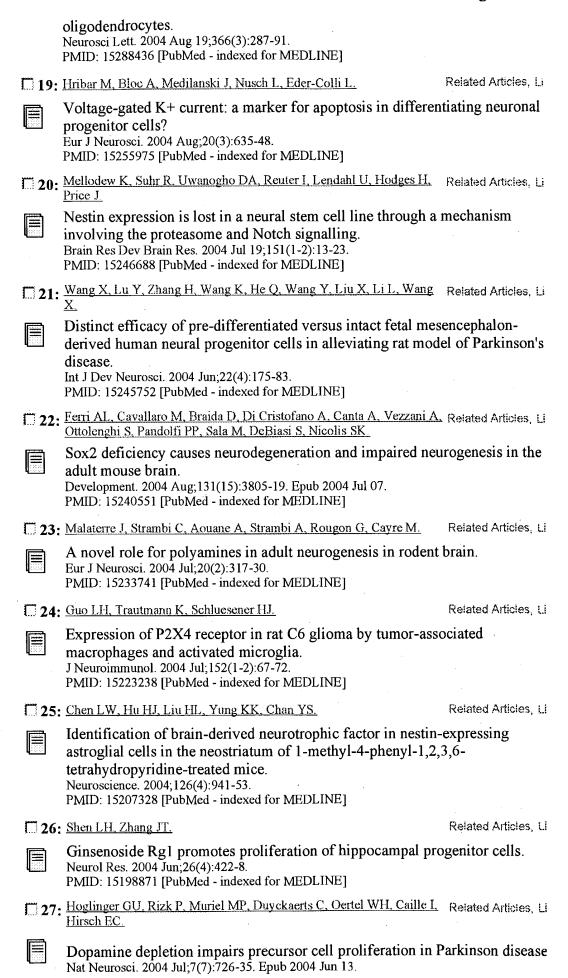
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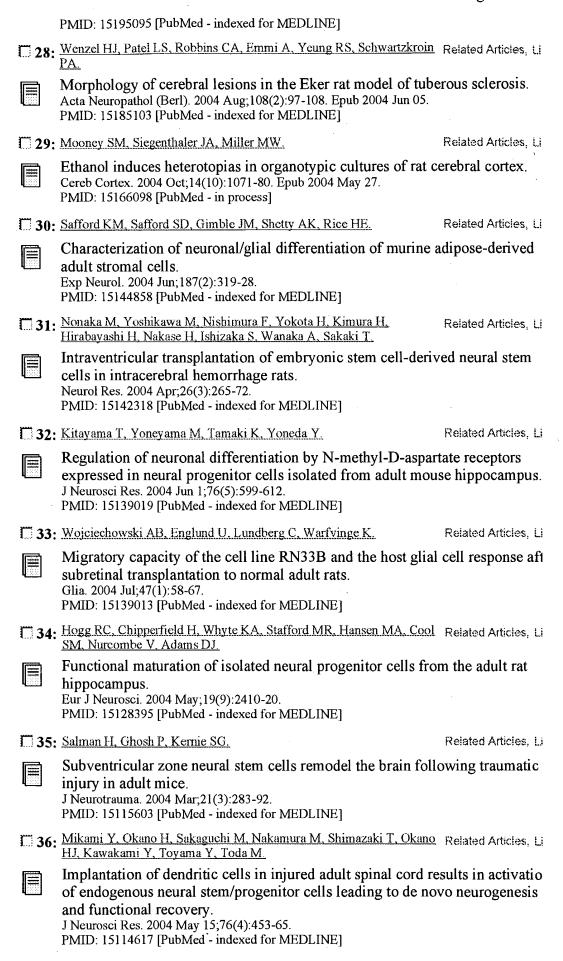
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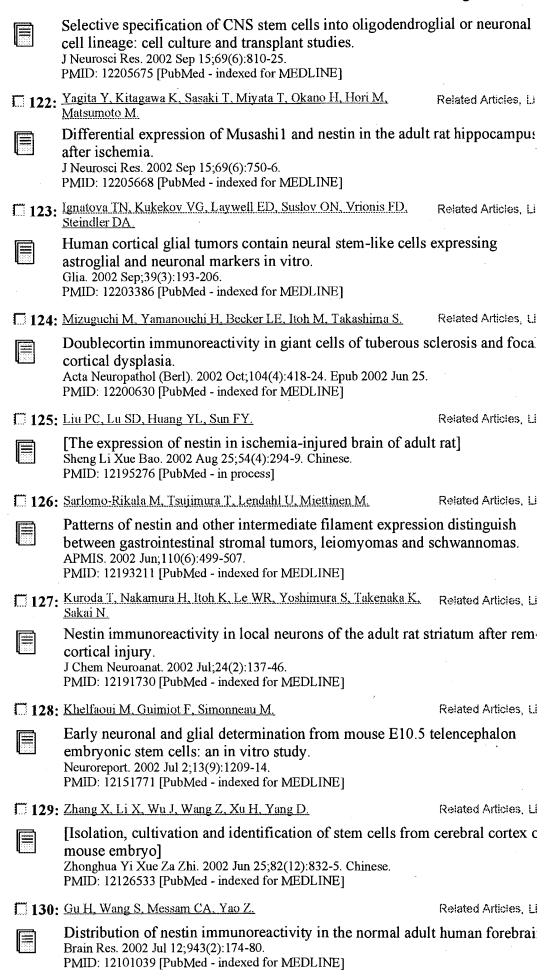
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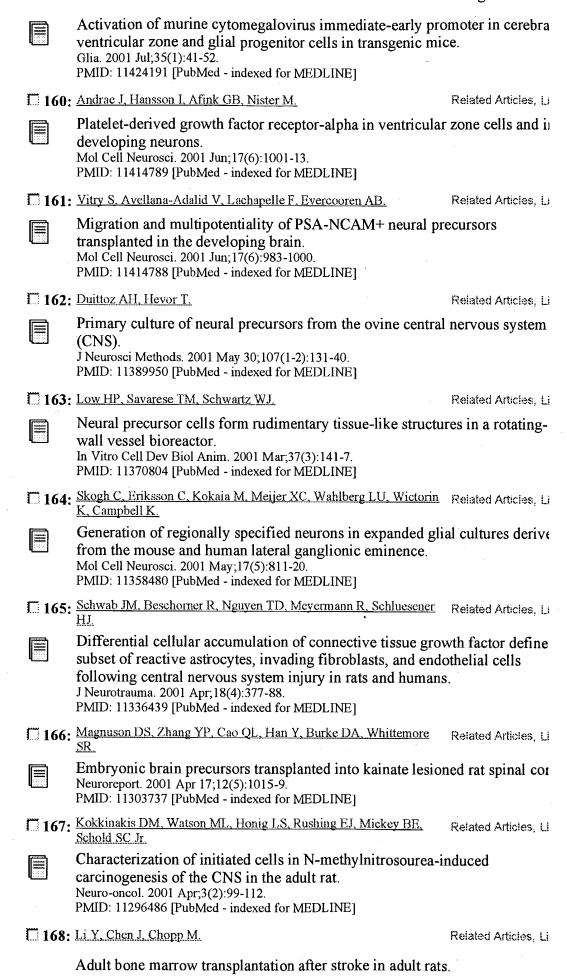
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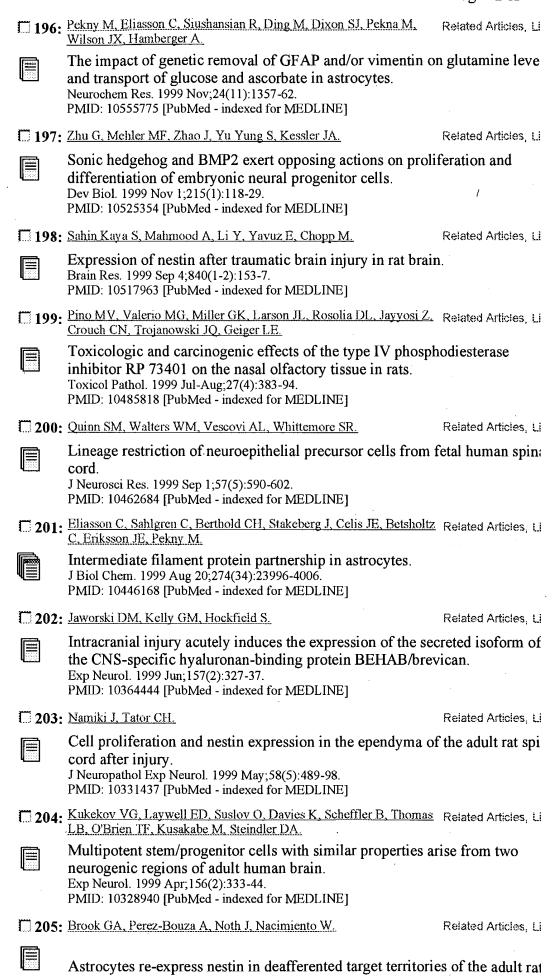
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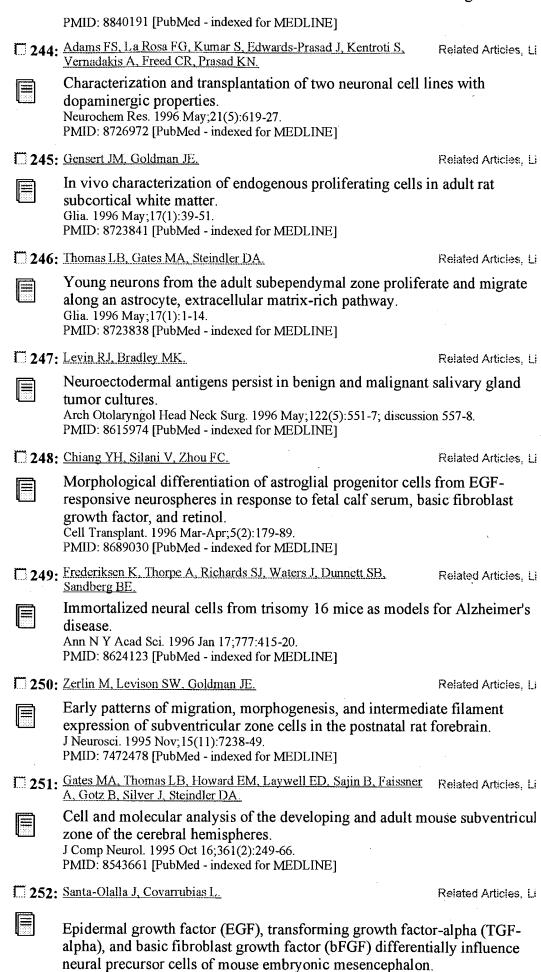
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Generation of neurons and astrocytes from isolated cells of the ad mammalian central nervous system.

Reynolds BA, Weiss S.

Department of Pathology, University of Calgary Faculty of Medicine, Alberta, Canada.

Neurogenesis in the mammalian central nervous system is believed to end in the period just after birth; in the mouse striatum no new neurons are produced after the first few days after birth. In this study, cells isolated from the striatum of the adult mouse brain were induced to proliferate in vitro by epidermal growth factor The proliferating cells initially expressed nestin, an intermediate filament foun in neuroepithelial stem cells, and subsequently developed the morphology and antigenic properties of neurons and astrocytes. Newly generated cells with neuronal morphology were immunoreactive for gamma-aminobutyric acid and substance P, two neurotransmitters of the adult striatum in vivo. Thus, cells of adult mouse striatum have the capacity to divide and differentiate into neurons and astrocytes.

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Reactive astrocytes express the embryonic intermediate neurofilament nestin.

Clarke SR, Shetty AK, Bradley JL, Turner DA.

Duke University Medical Center, Durham, NC.

Nestin is a neurofilament protein expressed by the immediate precursors to neurons and glia in rats and humans. Nestin immunoreactivity in the rat CNS v studied following kainic acid (KA) hippocampal lesions. Numerous nestin positive cells within the KA lesion were confirmed to be reactive astrocytes by their immunoreactivity for glial fibrillary acidic protein (GFAP). The number of these cells decreased with time after the KA lesion and no astrocyte immunostaining for nestin was observed in control animals. A subset of nestin positive cells in the ventricular subependymal region appeared to be radial gliacells, extending to cell body layers. Nestin is one of several embryonic marker expressed by reactive astrocytes, suggesting an embryonic reversion induced be the KA lesion, possibly to enhance functional recovery.

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Re-expression of the intermediate filament nestin in reactive astrocytes.

Lin RC, Matesic DF, Marvin M, McKay RD, Brustle O.

Department of Anatomy and Neurobiology, Medical College of Pennsylvania Hahnemann University, Philadelphia, PA 19102, USA.

The intermediate filament nestin is highly expressed in multipotential stem cel of the developing central nervous system (CNS). During neuro- and gliogenesi nestin is replaced by cell type-specific intermediate filaments, e.g. neurofilame and glial fibrillary acidic protein (GFAP). In this study, we demonstrate that nestin expression is re-induced in reactive astrocytes in the lesioned adult brain Following ischaemic and mechanical lesioning, a strong and sustained express of nestin was noted in GFAP-positive cells surrounding the lesion site. Lesion experiments in transgenic mice carrying the lacZ gene under control of regulat sequences from the nestin gene suggested that the upregulation of nestin in reactive astrocytes is mediated via the same sequences that control nestin expression during CNS development. These observations and recent data on th co-expression of glial and neuronal marker antigens in reactive astrocytes poin a close relationship between proliferating astrocytes and neuroepithelial precui cells. Copyright 1995 Academic Press, Inc.

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In vitro differentiation of embryonic stem cells into glial cells and functional neurons.

Fraichard A, Chassande O, Bilbaut G, Dehay C, Savatier P, Samarut J.

Laboratoire de Biologie Moleculaire et Cellulaire de l'ENS, UMR 49 CNRS, Ecole Normale Superieure de Lyon, France.

Mouse embryonic stem cells were induced to differentiate in culture with retin acid. Putative precursors of neurons and glial cells (nestin-positive cells) were clearly identified as early as three days after the onset of differentiation. At day neuron-like cells could be clearly identified, either as isolated cells or as cellul networks. Some of these cells were positive for astrocyte- or oligodendrocytespecific antigens (GFAP or O4 antigens, respectively). Other cells were positive for neuron-specific antigens (cytoskeleton proteins MAP2, MAP5 and NF200, well as synaptophysin). Some neuronal-like cells were also positive for acetylcholinesterase activity or glutamic acid decarboxylase expression, indicating that ES cells could differentiate into GABAergic and possibly cholinergic neurons. Electrophysiological analyses performed in voltage clami conditions showed that cell membranes contained voltage-dependent channels Overshooting action potentials could be triggered by current injection. Taken together, these data provide evidence that embryonic stem cells can differentia first into neuron-glia progenitors, and later into glial cells and functional neuro in vitro. This technique provides an unique system to study early steps of neuronal differentiation in vitro.

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In vitro differentiation of embryonic stem cells into glial cells and functional neurons.

Fraichard A, Chassande O, Bilbaut G, Dehay C, Savatier P, Samarut J.

Laboratoire de Biologie Moleculaire et Cellulaire de l'ENS, UMR 49 CNRS, Ecole Normale Superieure de Lyon, France.

Mouse embryonic stem cells were induced to differentiate in culture with retin acid. Putative precursors of neurons and glial cells (nestin-positive cells) were clearly identified as early as three days after the onset of differentiation. At day neuron-like cells could be clearly identified, either as isolated cells or as cellul networks. Some of these cells were positive for astrocyte- or oligodendrocytespecific antigens (GFAP or O4 antigens, respectively). Other cells were positive for neuron-specific antigens (cytoskeleton proteins MAP2, MAP5 and NF200, well as synaptophysin). Some neuronal-like cells were also positive for acetylcholinesterase activity or glutamic acid decarboxylase expression, indicating that ES cells could differentiate into GABAergic and possibly cholinergic neurons. Electrophysiological analyses performed in voltage clami conditions showed that cell membranes contained voltage-dependent channels Overshooting action potentials could be triggered by current injection. Taken together, these data provide evidence that embryonic stem cells can differentia first into neuron-glia progenitors, and later into glial cells and functional neuro in vitro. This technique provides an unique system to study early steps of neuronal differentiation in vitro.

PMID: 7593279 [PubMed - indexed for MEDLINE]

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## Erratum in:

• J Neurosci Res 1995 Dec 15;42(6):855.

Epidermal growth factor (EGF), transforming growth factor-alpl (TGF-alpha), and basic fibroblast growth factor (bFGF) differentially influence neural precursor cells of mouse embryonic mesencephalon.

Santa-Olalla J, Covarrubias L.

Departamento de Biologia Molecular, Universidad Nacional Autonoma de Mexico, Cuernavaca, Morelos, Mexico.

Growth factors are key elements in the process of neural cell differentiation. W examined the effects of classical mitogens on neural precursor cells, by culturi mouse cells of the embryonic (13.5 days postcoitum) mesencephalon and treat them with epidermal growth factor (EGF), transforming growth factor-alpha (TGF-alpha), basic fibroblast growth factor (bFGF), nerve growth factor (NGF and transforming growth factor-beta (TGF-beta). Our initial results show that EGF, TGF-alpha, or bFGF, but not NGF or TGF-beta, induced general proliferation of the cultured cells, followed by formation of colonies. Combinations of these three growth factors suggest that most cells with the capacity to form colonies responded to EGF, TGF-alpha, or bFGF. The numbe colonies increased significantly when EGF, but not TGF-alpha, was used in combination with bFGF. Furthermore, a population responding only to EGF + bFGF was detected in the dorsal mesencephalon. The colony-forming activity bFGF was dependent on insulin, but bFGF and insulin cooperation was indirect since we could not observe colony formation in subcultures of cells derived from colonies, even in the presence of insulin. Cells obtained from our colonies displayed neuronal and glial morphology and expressed markers of both neuro and astrocytes; nestin, a marker of neural precursor cells, was also expressed in the majority of colonies. Growth factors also influenced neuronal maturation; 1 best neurite outgrowth was obtained from cells derived from bFGF-induced colonies cultured in the presence of EGF + bFGF. These data indicate the existence of neural precursor cells in the embryonic mesencephalon that respon differentially to growth factors.

PMID: 8568917 [PubMed - indexed for MEDLINE]

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1: Cell Transplant. 1996 Mar-Apr;5(2):179-89. andrin kāl

Related Articles, I

FULL-TEXT ARTICLE

Morphological differentiation of astroglial progenitor cells from EGF-responsive neurospheres in response to fetal calf serum, bas fibroblast growth factor, and retinol.

Chiang YH, Silani V, Zhou FC.

Department of Anatomy, Indiana University School of Medicine, Indianapolis 46202, USA.

Procurement of multipotential neuroglial stem cells is possible with the additic of epidermal growth factor (EGF). Stem cells will differentiate into neurons ar. glia upon the removal of EGF from the culture medium. We have previously characterized the neuronal differentiation of stem cells derived from long-term cultured nonpassage neurospheres. In the current study, we (1) characterize the morphological differentiation of the astroglial progenitor cell from 3-mo-old neurospheres, (2) examine whether the astroglial progenitor cells from neurospheres of different brain areas exhibit different differentiation responses the same exogenous signals, and (3) test the effects of basic fibroblast growth factor (bFGF) and retinol on differentiation. Cerebral cortex, striatum, and mesencephalon cells were obtained from Embryonic Day 14 (E-14) rat fetuses and were dissociated for the procurement of neurospheres in chemically define medium supplemented with EGF. After 3 mo in culture, the neurospheres, derived from each of the three brain areas, were subcultured into three groups chamber slides: (1) basal medium, (2) the basal medium plus 20 ng/mL bFGF, and (3) the basal medium plus 10 muM retinol. Phenotypic expression of astroglial cells was examined after 14 days subculture. Our findings indicate the the 3-mo-old cultured nonpassage neurospheres contained numerous multipotential stem cells that stained positive with nestin, and that environmen factors played an important role in influencing the differentiation of astroglial progenitor cells. As detected by glial fibrillary acid protein (GFAP), astroglial progenitor cells turned into protoplasmic astrocytes in the FCS-containing basi medium, fibrous astrocytes in the presence of bFGF, and spindle-shaped astrocytes in the presence of retinol. There were no noticeable differences in differentiation among astroglial progenitor cells of the various brain regionderived neurospheres in any of the three medium conditions. Peculiar varicosit and growth cone-like structures on the long slender GFAP-positive processes suggest that neuroblasts and glioblast may share common morphologies, feature or common progenitor cells during initial differentiation in vitro.

PMID: 8689030 [PubMed - indexed for MEDLINE]

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Young neurons from the adult subependymal zone proliferate and migrate along an astrocyte, extracellular matrix-rich pathway.

Thomas LB, Gates MA, Steindler DA.

Department of Anatomy and Neurobiology, College of Medicine, University o Tennessee, Memphis 38163, USA.

The subependymal zone (SEZ) of the lateral ventricle of adult rodents has long been known to be mitotically active. There has been increased interest in the S since it has been demonstrated that neuroepithelial stem cells residing there generate neurons in addition to glia in vitro. In the present study, we have examined parasagittal sections of the adult mouse brain using immunocytochemistry for extracellular matrix (ECM) molecules (tenascin and chondroitin sulfate-containing proteoglycans), glial fibrillary acidic protein (GFAP, a cytoskeletal protein prominently expressed by immature and reactive astrocytes), RC-2 (a radial glial and immature astrocyte cytoskeletal marker), TuJ1 (a class III beta-tubulin isoform expressed solely by postmitotic and adul neurons), nestin (a cytoskeletal protein associated with stem cells), neuronspecific enolase, and bromodeoxyuridine (BrdU, which is taken up by dividing cells). Our results demonstrate that a population of young neurons reside withi an ECM-rich, GFAP-positive astrocyte pathway from the rostral SEZ all the w into the olfactory bulb. Furthermore, BrdU labeling studies indicate that there is high level of cell division along the entire length of this path, and double-label studies indicate that neurons committed to a neuronal lineage (i.e., TuJ1+) take BrdU (suggesting they are in the DNA synthesis phase of the cell cycle), again along the entire length of the SEZ "migratory pathway." Thus, the SEZ appear retain the ability to produce neurons and glia throughout the life of the animal, functioning as a type of "brain marrow." The implications of these findings are discussed in relation to the role that such a glial/ECM-rich boundary (as seen: the embryonic cortical subplate and other developing areas) may play in: confining the migratory populations and maintaining them in a persistent state immaturity; facilitating their migration to the olfactory bulb, where they are incorporated into established adult circuitries; and potentially altering SEZ cel. cycle dynamics that eventually lead to cell death.

PMID: 8723838 [PubMed - indexed for MEDLINE]

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Characterization and transplantation of two neuronal cell lines w dopaminergic properties.

Adams FS, La Rosa FG, Kumar S, Edwards-Prasad J, Kentroti S, Vernadakis A, Freed CR, Prasad KN.

Department of Medicine, University of Colorado Health Sciences Center, Den 80262, USA.

Immortalized rat mesencephalic cells (1RB3AN27) produced dopamine (DA) level that was higher than produced by undifferentiated or differentiated murin neuroblastoma cells (NBP2) in culture. Treatment of 1RB3AN27 and NBP2 ce with a cAMP stimulating agent increased tyrosine hydroxylase (TH) activity a the intensity of immunostaining for the DA transporter protein (DAT). 1RB3AN27 cells were labelled with primary antibodies to neuron specific enolase (NSE) and nestin and exhibited very little or no labeling with anti-glia fibrillary acidic protein (GFAP). 1RB3AN27 cells exhibited beta- and alphaadrenoreceptors, and prostaglandin E1 receptors, all of which were linked to adenylate cyclase (AC). Dopamine receptor (D1) and cholinergic muscarinic receptors linked to AC were not detectable. The levels of PKC alpha and PKC beta isoforms were higher than those of PKC gamma and PKC delta in 1RB3AN27 cells. The 1RB3AN27 cells were more effective in reducing the ra of methamphetamine-induced turning in rats with unilateral 6-OHDA lesion of the nigrostriatal system than differentiated NBP2 cells. The grafted 1RB3AN2 were viable as determined by DiI labelling, but they did not divide and did not produce T-antigen protein; however, when these grafted cells were cultured in vitro, they resumed production of T-antigen and proliferated after the primary cells and neurons of host brain died due to maturation and subsequent degeneration. Examination of H&E stained sections of the grafted sites reveale no evidence of infiltration of inflammatory cells in the grafted area suggesting that these cells were not immunogenic. They also did not form tumors.

PMID: 8726972 [PubMed - indexed for MEDLINE]

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1: Int J Dev Biol. 1996 Jun;40(3):591-7.

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## A neural precursor cell line derived from murine teratocarcinoma

## Hasgekar N, Saranath D, Seshadri R, Krishnaveni L, Ghosh S, Lalitha VS

Neuro-Oncology Division, Tata Memorial Centre, Parel, Bombay, India.

A cell line NT with phenotypic features of neural precursor cells has been established from an embryo-derived teratocarcinoma in Swiss mouse where, or serial transplantation, the developmental potential becomes restricted to neural pathway. All the cells are positive for nestin (a marker of neuroepithelial stem cells). Many of them are also positive for NFP and/or GFAP. Moreover there i gradual decrease from 75% to 50% in reactivity for alkaline phosphatase, a marker for EC cells with repeated passages. The bipotential nature, and the probable decline of EC cells suggest that NT is a neural precursor cell line. Th cells have doubling time of 12 h with a plating efficiency of 50%. The cells for colonies in soft agar within 7 days and tumorigenicity in syngeneic mice is los after 70th passage. However, after 70 passages cells do form tumors in nude m within 5 days and these tumors exhibit better differentiated morphology than tl tumors in syngeneic mice. All the other characteristics remain stable. The myc and ras family of oncogenes do not show any alterations in early or late passag This cell line may therefore be considered as a differentiated cell line derived from teratocarcinoma.

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1: Exp Neurol. 1996 Sep; 141(1):67-78.

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FULL-TEXT ARTICLE Expression of neuronal antigens by astrocytes derived from EGF generated neuroprogenitor cells.

Schinstine M, Iacovitti L.

Department of Neurobiology & Anatomy, Medical College of Pennsylvania, Philadelphia, USA.

Previous studies have demonstrated that astrocytes reacting to CNS injury can express antigens normally associated with neurons. The origin of the reactive astrocytes, i.e., whether they are newly differentiated glial cells or preexisting astrocytes somehow triggered to express neuronal markers, remains difficult to determine using an in vivo model system. An in vitro model may prove more manageable. In the present study, primary brain cultures and EGF-generated neuroprogenitor cells were used to study the expression of neuronal antigens b established (primary) and nascent astrocytes, respectively. Astrocytes derived directly from dissociated mouse brains exhibited a flat morphology typical of t 1 astrocytes. These cells were nestin and GFAP positive and, in most cases, the antigens were colocalized. Primary astrocytes did not appear to express the putative neuronal markers GABA, Tau, or MAP2. Nascent astrocytes derived from EGF-generated progenitor cells showed a similar pattern of GFAP and nestin immunoreactivity. Contrary to primary astrocytes, many GFAP-intensiv stellate astrocytes exhibited Tau and MAP2. These cells also exhibited an internestin immunoreactivity. These data suggest that the reactive astrocytes expressing neuronal antigens in response to CNS trauma may be derived from neural progenitor cells rather than from previously differentiated astrocytes.

PMID: 8797669 [PubMed - indexed for MEDLINE]

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FULL-TEXT ARTICLE

Expression of neuronal antigens by astrocytes derived from EGFgenerated neuroprogenitor cells.

Schinstine M, Iacovitti L.

Department of Neurobiology & Anatomy, Medical College of Pennsylvania, Philadelphia, USA.

Previous studies have demonstrated that astrocytes reacting to CNS injury can express antigens normally associated with neurons. The origin of the reactive astrocytes, i.e., whether they are newly differentiated glial cells or preexisting astrocytes somehow triggered to express neuronal markers, remains difficult to determine using an in vivo model system. An in vitro model may prove more manageable. In the present study, primary brain cultures and EGF-generated neuroprogenitor cells were used to study the expression of neuronal antigens b established (primary) and nascent astrocytes, respectively. Astrocytes derived directly from dissociated mouse brains exhibited a flat morphology typical of t 1 astrocytes. These cells were nestin and GFAP positive and, in most cases, the antigens were colocalized. Primary astrocytes did not appear to express the putative neuronal markers GABA, Tau, or MAP2. Nascent astrocytes derived from EGF-generated progenitor cells showed a similar pattern of GFAP and nestin immunoreactivity. Contrary to primary astrocytes, many GFAP-intensiv stellate astrocytes exhibited Tau and MAP2. These cells also exhibited an internestin immunoreactivity. These data suggest that the reactive astrocytes expressing neuronal antigens in response to CNS trauma may be derived from neural progenitor cells rather than from previously differentiated astrocytes.

PMID: 8797669 [PubMed - indexed for MEDLINE]

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**1:** Dev Neurosci. 1997;19(2):202-9.

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Developmental change of the nestin-immunoreactive midline rapl glial structure in human brainstem and spinal cord.

Takano T, Becker LE.

Department of Pathology, Hospital for Sick Children, Ont., Canada.

To elucidate the development of the midline raphe glial structure (MRGS) in human brainstem and spinal cord, immunohistochemistry was carried out in 10 developmentally normal brains (age range, 11 weeks postconception to 6 mont using antibodies to nestin and glial fibrillary acidic protein (GFAP). Nestin expression was most extensive in the youngest fetus (11 weeks postconception age, PCA), which showed strong immunoreactivity in radial glial fibers in the midline raphe and paramedian areas of brainstem and spinal cord. Nestinimmunoreactive radial glial fibers in the midline raphe gradually decreased in length and intensity, losing contact with the pial surface 20-24 weeks PCA. Radial glial cells in midbrain transformed into subependymal cells at 30 weeks PCA. Some fragments of radial fibers in brainstem and spinal cord could still be detected up to 30 weeks PCA. Weak GFAP immunoreactivity in the midline raphe was found in radial fibers in the dorsal midline of the midbrain and cervi spinal cord at 30 and 38 weeks PCA. This change of nestin positivity was thou to be due to the process remodeling the MRGS, not to the intracellular distribution and any identifiable clinical factors in the stillbirths. This irregular in the appearance of the MRGS supports its proposed role as a guide for cell migration, a potential source of new astrocytes, and a barrier to aberrant decussation of growing axons.

PMID: 9097036 [PubMed - indexed for MEDLINE]

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1: Brain Res Dev Brain Res. 1997 Feb 20;98(2):291-5.

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FULL-TEXT ARTICLE

Co-expression of MAP-2 and GFAP in cells developing from rat EGF responsive precursor cells.

Rosser AE, Tyers P, ter Borg M, Dunnett SB, Svendsen CN.

MRC Cambridge Centre for Brain Repair, Cambridge University Forvie Site, 1 aer23@hermes.cam.ac.uk

In this study we have performed a detailed analysis of EGF-responsive precurs as they develop into neurons and astrocytes using antibodies to nestin, microtubule-associated protein 2 (MAP-2c and MAP-2ab) and glial fibriallary acidic protein (GFAP). Surprisingly, at early time points, most GFAP-positive cells also stained for MAP-2c, and we postulate that this may be a normal stag astroglial development. At 7 days most of the cells had developed into astrocy and MAP-2ab-positive cells only represented 5% of the total neuronal populati This study shows that (i) MAP-2c is a marker for early precursors, (ii) the majority of cells developing from. EGF-responsive precursors develop into gli and (iii) only a small population of cells arising from expanded populations of EGF-responsive precursors develop into neurons expressing MAP-2ab. Thus, certain critical signals important for full neuronal differentiation may be missir from this system.

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☐ 1: Brain Res. 1997 Apr 4;753(1):18-26.

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Isolation, cloning and characterization of a putative type-1 astroc cell line.

Seidman KJ, Teng AL, Rosenkopf R, Spilotro P, Weyhenmeyer JA.

Neuroscience Program, University of Illinois, Urbana 61801, USA.

We have established a permanent cell line (1H91) of putative type-1 astrocyte precursor cells that were clonally derived from a single cell isolated from E16 mouse cerebellum. Epidermal growth factor (EGF) and transforming growth factor (TGF alpha) are strong mitogens for 1H91 cells (ED50 of 9.02 + 1.74 ng/ml and 15.98 +/- 2.34 ng/ml, respectively), while basic fibroblast growth factor (bFGF) is only weakly mitogenic and platelet derived growth factor (PDGF) has no mitogenic activity. In the proliferative state, the 1H91 cells are immunohistochemically positive for nestin and vimentin, and negative for A2I CNPase, neurofilament (NF), and neuron specific enolase (NSE). The majority EGF-treated 1H91 cells are not immunoreactive for glial acid fibrillary protein (GFAP). In the presence of 5 ng/ml bFGF, 1H91 cells become non-mitotic and develop a morphology consistent with a fibrous astrocyte. In contrast to the proliferating cultures, the bFGF treated cultures were strongly immunoreactive for GFAP, only mildly immunoreactive for nestin and vimentin, and negative 1 A2B5, CNPase, NF, and NSE. Type-1 astrocytes are known to proliferate in response to EGF, and are immunohistochemically GFAP positive, A2B5 negative, and CNPase negative [38]. However, type-1 astrocytes only develop fibrous morphology during the process of reactive gliosis [31]. Since EGF is a strong mitogen for 1H91 cells, and these cells may be differentiated into GFA1 positive, A2B5 negative, CNPase negative astrocytes, we conclude that 1H91 cells conform to a type-1 astrocyte precursor phenotype. In addition, the fibrou morphology of the bFGF treated 1H91 cells suggests that these cells follow the process of reactive gliosis. Therefore, the 1H91 clonal cell line may provide ar vitro model for studying the underlying cellular mechanisms of the type-1 astrocyte in reactive gliosis.

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1: J Neurosci Res. 1997 Apr 15;48(2):83-94.

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Multipotential and lineage restricted precursors coexist in the mammalian perinatal subventricular zone.

Levison SW, Goldman JE.

Department of Neuroscience and Anatomy, Pennsylvania State University College of Medicine, Hershey, USA.

Developmental studies have shown that both neurons and glia arise from the subventricular zone (SVZ) but there have been no clonal analyses to determine whether a single progenitor can produce both. Therefore, we used replication deficient retroviral vectors to analyze the clonal progeny of single rat SVZ cell that were maintained in culture media permissive or non-permissive for neuror differentiation. When maintained in medium supplemented with 5% fetal bovi serum, all surviving progenitors generated glial cell clones. Within these glial clones we often observed both type 1 astrocytes and O-2A lineage cells. When SVZ cells were maintained in medium permissive for neurogenesis approxima 50% of the total clones contained at least one antigenically defined neuron. Of those clones that contained neurons, 60% contained neurons and glia. The other 50% of the total clones were either comprised of only astrocytes, astrocytes an oligodendrocytes, or were unidentifiable. Since the culture environment permir multilineage clone formation, yet many homogeneous neuronal or astrocytic clones were obtained, some progenitors must become developmentally restrict while they are in the germinal zone. Therefore, we conclude that the perinatal SVZ is a mosaic of multipotential, bipotential, and lineage restricted precursor and that the lack of postnatal neocortical neurogenesis is not due to the absence potential neuroblasts.

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Neuroepithelial stem cells from the embryonic spinal cord: isolati characterization, and clonal analysis.

Kalyani A, Hobson K, Rao MS.

Department of Neurobiology and Anatomy, University of Utah School of Medicine, Salt Lake City 84132, USA.

Adherent cultures of E10.5 rat neuroepithelial cells (NEP cells) from the cauda neural tube require FGF (fibroblast growth factor) and CEE (chick embryo extract) to proliferate and maintain an undifferentiated phenotype in culture. Epidermal growth factor (EGF) does not support E10.5 NEP cells in adherent culture and NEP cells do not form EGF-dependent neurospheres. NEP cells, however, can be grown as FGF-dependent neurospheres. NEP cells express ne and lack all lineage-specific markers for neuronal and glial sublineages, retain their pleuripotent character over multiple passages, and can differentiate into neurons, astrocytes, and oligodendrocytes when plated on laminin in the absen of CEE. In clonal culture, NEP cells undergo self-renewal and generate colonithat vary in size from single cells to several thousand cells. With the exception a few single-cell clones, all other NEP-derived clones contain more than one identified phenotype, with over 40% of the colonies containing A2B5, beta-11 tubulin, and GFAP-immunoreactive cells. Thus, NEP cells are multipotent and capable of generating multiple neural derivatives. NEP cells also differentiate motoneurons immunoreactive for choline acetyl transferase (ChAT) and the lo affinity neurotrophin receptor (p75) in both mass and clonal culture. Double labeling of clones for ChAT and glial, neuronal, or oligodendrocytic lineage markers shows that motoneurons always arose in mixed cultures with other differentiated cells. Thus, NEP cells represent a common progenitor for motoneurons and other spinal cord cells. The relationship of NEP cells with ot neural stem cells is discussed.

PMID: 9205140 [PubMed - indexed for MEDLINE]

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Ultrastructure of intermediate filaments of nestin- and vimentinimmunoreactive astrocytes in organotypic slice cultures of hippocampus.

Miyaguchi K.

Laboratory of Neurobiology, NINDS, NIH, Bethesda, Maryland 20892, USA.

Glial cells in rat hippocampal slices cultured for 4 weeks were examined with immunocytochemical and cryoelectron microscopical methods. Astrocytes possessing long processes were similarly stained with antibodies against nestir vimentin, and glial fibrillary acidic protein as seen by confocal microscopy. The three antibodies also labeled intermediate filaments in these astrocytes. In orde examine the fine structure of these intermediate filaments, slices were rapidfrozen for freeze-substitution and freeze-etching. By freeze-substitution the processes of the astrocytes were packed with large hundles of intermediate filaments. In rapid-freeze deep-etched slices, these filaments were often interconnected with filamentous cross-bridges. These cross-bridges were rathe uniform in size and shape (mean 2.9 nm thick and 14.8 nm long). These results suggest that the filament network with these cross-linkers is important for shar the long processes of nestin- and vimentin-immunoreactive astrocytes in slice cultures.

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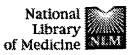
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1: Exp Neurol. 1997 Nov;148(1):147-56.

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In vitro cell density-dependent clonal growth of EGF-responsive murine neural progenitor cells under serum-free conditions.

Hulspas R, Tiarks C, Reilly J, Hsieh CC, Recht L, Quesenberry PJ.

Department of Cell Biology, University of Massachusetts Medical Center, Worcester, USA.

Neural progenitor cell populations responsive to epidermal growth factor (EGI have been shown to have proliferative potential and give rise to neurons. astrocytes, and oligodendrocytes. We have characterized EGF-responsive neur progenitor cells that give rise to bilineage neuronal/glial colonies (colony-form unit neuron-glia; CFU-NeGl) and unilineage neuronal colonies (CFU-Ne). Clonality was confirmed utilizing mixtures of brain cells from Balb/c and ROSA26 (transgenic for beta-galactosidase) mice. With a few exceptions, colonies showed either all blue cells or all clear cells after staining with X-Gal Clonal growth was analyzed after 10-11 days in relation to cell density by determining colony size and plating efficiency. Growth was density dependent (no growth below 10,000 cell/ml) and thus single cell cloning was not accomplished. An average plating efficiency of 4% was found for EGFresponsive neural cells derived from day 15-18 murine embryos when cultured 12,500 to 200,000 cells/ml. Similar results were obtained with 1-day-old postn neural cells. When colonies were categorized by size, the relative number of colonies over 50 cells appeared to be maximum at 50,000 plated cells/ml. Afte 11 days in culture, 94, 96, and 78% of the colonies contained cells that express nestin, neurofilament, and GFAP, respectively. Double-label experiments revealed that > 62% of the colonies contained both GFAP and neurofilament expressing cells. These studies establish the existence of at least two population of clonal neural progenitors: CFU-Ne and CFU-NeGl in fetal and postnatal murine brain.

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In vitro cell density-dependent clonal growth of EGF-responsive murine neural progenitor cells under serum-free conditions.

Hulspas R, Tiarks C, Reilly J, Hsieh CC, Recht L, Quesenberry PJ.

Department of Cell Biology, University of Massachusetts Medical Center, Worcester, USA.

Neural progenitor cell populations responsive to epidermal growth factor (EGI have been shown to have proliferative potential and give rise to neurons, astrocytes, and oligodendrocytes. We have characterized EGF-responsive neur progenitor cells that give rise to bilineage neuronal/glial colonies (colony-form unit neuron-glia; CFU-NeGl) and unilineage neuronal colonies (CFU-Ne). Clonality was confirmed utilizing mixtures of brain cells from Balb/c and ROSA26 (transgenic for beta-galactosidase) mice. With a few exceptions, colonies showed either all blue cells or all clear cells after staining with X-Gal Clonal growth was analyzed after 10-11 days in relation to cell density by determining colony size and plating efficiency. Growth was density dependent (no growth below 10,000 cell/ml) and thus single cell cloning was not accomplished. An average plating efficiency of 4% was found for EGFresponsive neural cells derived from day 15-18 murine embryos when cultured 12,500 to 200,000 cells/ml. Similar results were obtained with 1-day-old postn neural cells. When colonies were categorized by size, the relative number of colonies over 50 cells appeared to be maximum at 50,000 plated cells/ml. Afte 11 days in culture, 94, 96, and 78% of the colonies contained cells that express nestin, neurofilament, and GFAP, respectively. Double-label experiments revealed that > 62% of the colonies contained both GFAP and neurofilament expressing cells. These studies establish the existence of at least two populatio of clonal neural progenitors: CFU-Ne and CFU-NeGl in fetal and postnatal murine brain.

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A nestin-negative precursor cell from the adult mouse brain gives rise to neurons and glia.

Kukekov VG, Laywell ED, Thomas LB, Steindler DA.

Department of Anatomy and Neurobiology, The University of Tennessee, Memphis 38163, USA.

Using a novel suspension culture approach, previously undescribed population of neural precursor cells have been isolated from the adult mouse brain. Recen studies have shown that neuronal and glial precursor cells proliferate within th subependymal zone of the lateral ventricle throughout life, and a persistent expression of developmentally regulated surface and extracellular matrix molecules implicates cell-cell and cell-substrate interactions in the proliferation migration, and differentiation of these cells. By using reagents that may affect cell-cell interactions, dissociated adult brain yields two types of cell aggregate; type I and type II spheres. Both sphere types are proliferative, and type I sphere evolve into type II spheres. Neurons and glia arise from presumptive stem cells type II spheres, and they can survive transplantation to the adult brain.

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Incorporation and glial differentiation of mouse EGF-responsive neural progenitor cells after transplantation into the embryonic r brain.

Winkler C, Fricker RA, Gates MA, Olsson M, Hammang JP, Carpenter N Bjorklund A.

Wallenberg Neuroscience Center, Lund University, Lund, S-22362, Sweden.

In vitro, epidermal growth factor (EGF)-responsive neural progenitor cells exh multipotent properties and can differentiate into both neurons and glia. Using a in utero xenotransplantation approach we examined the developmental potentiof EGF-responsive cells derived from E14 mouse ganglionic eminences, cortic primordium, and ventral mesencephalon, after injection into the E15 rat forebr ventricle. Cell cultures were established from control mice or from mice carryi the lacZ transgene under control of the promoters for nestin, glial fibrillary aci protein (GFAP), or myelin basic protein (MBP). The grafted cells, visualized v mouse-specific markers or staining for the reporter gene product, displayed widespread incorporation into distinct forebrain and midbrain structures and differentiated predominantly into glial cells. The patterns of incorporation of c from all three regions were very similar without preference for the homotopic brain areas. These results suggest that EGF-responsive progenitor cells can respond to host derived environmental cues, differentiate into cells with glial-l features, and become integrated in the developing recipient brain. Copyright 1! Academic Press.

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Long-term nonpassaged EGF-responsive neural precursor cells a stem cells.

Zhou FC, Chiang YH.

Department of Anatomy and Program of Medical Neurobiology, Indiana University School of Medicine, Indianapolis, Ind, USA.

We have screened lines of nonpassaged epidermal growth factor-responsive neurospheres from embryonic striatum and brainstem. They have been maintained in defined medium with epidermal growth factor over a period of 2 years and remained in an undifferentiated state to this date. Since isolation from the brain 2 years ago, these nonpassaged epidermal growth factor responsive neurospheres have shown active proliferation and self-renewal capacity. When subplated on a poly-D-lysine coated surface, they resumed differentiation with 24 hours. The differentiation process of the nonpassaged epidermal growth fac responsive neurosphere appeared to recapitulate the neural development in the brain. Many cells migrated, extending radial processes while expressing nesting and S100 in the early 7-day subplating culture. They continued to differentiate into major neural types in 14-day subplating culture, including fibrous and cytoplasmic astrocytes, oligodendrocytes, and serotonin, gamma-aminobutyric acid, and a small number of tyrosine hydroxylase-positive neurons. The nonpassaged epidermal growth factor-responsive neurospheres in many ways resemble hemopoietic cells. Both are proliferative, possess the potential of indefinite self-renewal, yet multipotent, and are capable of resuming the differential pathway. The nonpassaged epidermal growth factor responsive neurospheres meet the criteria of stem cells and have been found to be a useful model to study the development in vitro.

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       US 2004161419
       Utility; Patent Application - First Publication
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       CHEMICAL
       APPLICATION
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GΙ
        12 Figure(s).
      FIG. 1 is a bar graph showing that the cultured placental stem cells
       express characteristic embryonic stem cell surface markers: stage
       specific embryonic antigen 3 and 4 (SSEA-3, SSEA4); tumor related antigen
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1-60 (TRA 1-60); TRA 1-81, thymidylate synthase complementing protein (Thy-1) and the proto-oncogene tyrosine-protein kinase kit (c-kit).

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significantly better in the presence of Epidermal Growth Factor ***EGF*** ) (10 ng/ml (square)) than in the absence of ***E
ng/ml (circle)).
FIG. 3 is a light micrograph showing placental stem cells cultured for 14
days in the absence (w/o ***EGF*** ) or presence of ***EGF*** 10
   nq/ml.
FIG. 4 is a gel showing the placental stem cells cultured for 0 and 24 days with Epidermal Growth Factor ( ***EGF*** ) 10 ng/ml continue to
uays with Epidermal Growth Factor ( ***EGF*** ) 10 ng/ml continue to express characteristic stem cell markers: Octamerbinding transcription factor-4 (also known as OCT-3/4); Sex determining region Y related-HMG box 2 (SOX2); left-right determination factor A (Lefty-A); fibroblast growth factor 4 (FGF-4); Rex-1 (also known as zinc finger protein-42 (ZFP-42)) and teratocarcinoma-derived growth factor-1 (TDGF-1).

FIG. 5 are micrographs showing phase contrast images (A, C, E, G, I) and immunofluorescent images (B, D, F, H, J) of embryoid body (EB) like structures formed by culturing placental stem cells to 80% confluence in media containing 10% Fetal Bovine Serum and ***EGF*** 10 ng/ml prior to transferring such cells onto a 20% (v/v) Matrigel coated plate. FIG
    to transferring such cells onto a 20% (v/v) Matrigel coated plate; FIG.
   5(B) shows immunohistofluorescent staining of placental stem cells with antibodies against alkaline phosphatase; FIG. 5(D) shows immunohistofluorescent staining of placental stem cells with antibodies against stage specific embryonic antigen antibody-3 (SSEA-3); FIG. 5(F) shows immunohistofluorescent staining of placental stem cells with antibodies against stage specific embryonic antigen antibody-3 (SSEA-3); FIG. 5(F) shows immunohistofluorescent staining of placental stem cells with
    antibodies against stage specific embryonic antigen antibody-4 (SSEA-4);
   FIG. 5(H) shows immunohistofluorescent staining of placental stem cells with antibodies against tumor related antigen 1-60 (TRA 1-60); FIG. 5(J)
   shows immunohistofluorescent staining of placental stem cells with antibodies against tumor related antigen 1-81 (TRA 1-81).
FIG. 6 are micrographs showing immunohistochemical staining of human placental tissue (left panel) and placental stem cells (right panel) with antibodies against cytokeratin AE1/AE3, cytokeratin 19 (CK19), cytokeratin 18 (CK18), the protooncogene tyrosine-protein kinase kit
    (c-kit), thymidylate synthase complementing protein (Thy-1), alpha-1-antitrypsin (AlAT), and alpha fetoprotein (AFP).
 FIG. 7 is a bar graph showing the relative differences in RNA expression
    of various liver-specific markers in the placental stem cells of the
present invention as compared to those described in Sakuragawa et al (Sakuragawa et al., J Hum Genet. 45:171-176 (2000)).

FIG. 8(A) is a bar graph showing the induction of hepatocyte specific mRNA (albumin, alpha-1-antitrypsin (A1AT), and C/EBPalpha) in placental stem cells cultured for 0, 3, 9 and 15 days on Type-I collagen coated plates supplemented with dexamethasone (0.1 mu M), insulin (0.1 mu M) and phenobarbital (1 mM). FIG. 8(B) are micrographs showing
    phenobarbital (1 mM); FIG. 8(B) are micrographs showing
    immunohistochemistry staining of hepatocytes derived from placental stem
   cells using antibodies against human albumin (upper panels), and antibodies against hepatocyte nuclear factor-4 alpha (HNF-4 alpha) (lower left panel). The lower right panel shows a phase contrast image of hepatocytes derived from placental stem cells; FIG. 8(C) is a bar graph showing that hepatocytes derived from placental stem cells exhibit cytochrome P450 (CPY1A1/CPY1A2) activity upon beta-naphthoflavone (50 mu M) induction at levels that are approximately 60% of the activity of freshly isolated human hepatocytes. CPY1A1/CPY1A2 activity was measured
    freshly isolated human hepatocytes. CPY1A1/CPY1A2 activity was measured
    using an ethoxyresorufin-o-deethylase (EROD) assay; FIG. 8(D) is a chromatogram of a high pressure liquid chromatographic (HPLC) separation
    of testosterone metabolite, 6-beta-hydroxy testosterone, generated in hepatocytes derived from placental stem cells.
 FIG. 9(A) are fluorescent micrographs showing placental stem cells expressing glial fibrillary acid protein ( ***GFAP*** ), C-type natriuretic peptide (CNP) and beta-tubulin III; FIG. 9(B) is a gel showing the placental stem cells cultured for 0 and 7 days in media
    supplemented with all-trans retinoic acid express neural specific markers such as ***nestin*** , neuron specific enolase (NSE), neurofilament-M
 supplemented with all-trans retinoic acid express neural specific markers such as ***nestin*** , neuron specific enolase (NSE), neurofilament-M (NF-M), glutamic acid decarboxylase (GAD) , glial fibrillary acid protein (***GFAP*** ), and myelin basic protein (MBP).

FIG. 10 are light and electron micrographs showing vascular endothelial cells generated from placental stem cells cultured on Matrigel (TM).

FIG. 11 is a gel showing that placental stem cells cultured for 14 days in media supplemented with nicotinamide (10 mM) express pancreatic cell specific markers such as insulin, glucagon, homeobox transcription factor Nkx-2.2, paired box gene 6 (Pax6) and pancreatic duodenal homeobox 1 (Pdx1).
  FIG. 12(A) is a gel showing that placental stem cells cultured for 0 and
     14 days in media supplemented with ascorbic acid 2 phosphate (1 mM)
     express cardiac specific markers such as cardiac transcription factor-4
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(GATA-4), cardiogenic homeodomain factor Nkx 2.5, atrial myosin light

human atrial natriuretic peptide (hANP), and cardiac troponin T (cTnT); FIG. 12(B) is an immunofluorescent micrograph showing actinin expression in cardiomyocytes derived from placental stem cells.

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          ANSWER 3 OF 313
L5
            10614236 IFIPAT; IFIUDB; IFICDB
ΝA
            DIFFERENTIATION OF STEM CELLS TO PANCREATIC ENDOCRINE CELLS
TI
            Blondel Oliver; Kim Jong-Hoon; Lumelsky Nadya L; McKay Ronald D
Unassigned Or Assigned To Individual (68000)
IN
PA
            US 2004121460
US 2002-470030
                                                     20040624
                                            A1
PΙ
                                                     20020124
AΙ
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            WO 2002-US2361
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            US 2004121460
FI
             Utility; Patent Application - First Publication
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             CHEMICAL
            APPLICATION
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              5 Figure(s)
GΙ
           FIG. 1 is a diagram of one protocol for the differentiation of ES cells to
            pancreatic endocrine cells.
           FIG. 2 is a digital image showing insulin-producing cells differentiated
             from embryonic stem cells contain different hormone-producing cell types
             and are organized in threedimensional clusters with topological
             organization of pancreatic islets. FIG. 2A shows an inner core of insulin
            cells (grey) surrounded by an outer layer of glucagon producing cells (white). FIG. 1B is a digital image showing an inner core of insulin producing cells (grey) surrounded by an outer layer of somatostain producing cells (white).
           FIG. 3 is a set of graphs and figures demonstrating that islet clusters
             release insulin in response to glucose utilizing normal pancreatic
            mechanisms. FIG. 3A is a graph of insulin release in response to different glucose concentrations. Exposure to 50 mM sucrose was used to
            test for a potential effect of high osmolarity on insulin release. FIG. 3B is a diagrammatic summary of the documented actions of glucose, cAMP, K+ and Ca2+ on insulin secretion. Effects of known pharmacological regulators of insulin release are indicated. DAG, diacylglycerol; PKA, protein kinase A; PKC, protein kinase C; PLC, phospholipase C. FIG. 3C is a schematic diagram of insulin release in response to various secretaguogues in the presence of 5 mM of glucose. FIG. 3D is a set of bar graphs showing insulin release in response to 20 MM glucose in the presence or absence of inhibitors of insulin secretion.
             presence or absence of inhibitors of insulin secretion.
           FIG. 4 is a diagram of the differentiation of pancreatic endocrine cells
             from pancreatic endocrine stem cells to differentiated alpha cells, beta
           cells, delta cells, and PP cells.
FIG. 5 is a set of panels showing the neural and pancreatic differentiation of ES cells. FIG. 1A is a set of digital images showing
             the cells during the procedure for induction of midbrain dopaminergic
            the cells during the procedure for induction of midbrain dopaminergic neurons from ES cells as previous described (see WO 01/83715, herein incorporated by reference). Briefly, the ES cells were taken through 5 steps or stages. In stage 1 undifferentiated ES cells were cultured for 5 days in the presence of 15% fetal calf serum (FCS) on gelatin coated tissue culture dishes in the presence of LIF (1,400 U/ml). In stage 2 embryoid bodies (Ebs) were generated in the presence of FCS for 4 days in the presence or absence of LIF (1,000 U/ml.). In stage 3, the EBs were plated into ITSFn medium (Okabe et al., Mech. Dev. 59: 89-102, 1996) where over 10 days ***Nestin*** + cells migrated from the cell aggregates. In stage 4 these ***Nestin*** + cells were resuspended and expanded for 4 days in N2 medium containing ***bFGF***, sonic hedgehog (Shh) and fibroblast growth factor-8 (FGF8). In stage 5 the
             hedgehog (Shh) and fibroblast growth factor-8 (FGF8). In stage 5 the medium was changed into N2 medium without ***bFGF*** , Shh or FGF
                                                                                                                                , Shh or FGF8.
             medium was changed into N2 medium without
             These cells differentiated efficiently into neurons and astrocytes over a two week period. Embryoid bodies were generated in the presence (LIF+) or absence (LIF-) of LIF (1000 U/ml) and differentiated.

Doubleimmunostaining for TuJ1/ ***GFAP*** (upper panels, day 8 in stage 5) and PDX-1/En-1 (lower panels, day 3 in stage 4). LIF treatment
             in stage 2 (EB formation) increases the neuronal (TuJ1+cells, light grey) and decreases the astrocytic ( ***GFAP*** +, dark grey) population. LIF
              treatment efficiently enhances midbrain precursor cells (En-1+ cells,
             dark grey) and negatively regulates pancreatic precursor cells (PDX-1+cells, light grey). FIG. 5C is a bar graph showing that the yield
              of En-1+ and PDX1+ cells is expressed as a percentage of total cells at
              stage 4.
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METHODS FOR INDUCING IN VIVO PROLIFERATION AND MIGRATION OF TRANSPLANTED
PROGENITOR CELLS IN THE BRAIN
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            Bjorklund Anders (SE)
IN
PA
            Unassigned Or Assigned To Individual (68000)
                                            A1 20040527
PΙ
            US 2004103448
ΑI
            US 2003-713373
                                                      20031113
RLI
            US 2000-693043
                                                      20001020 CONTINUATION
                                                                                                                        PENDING
                                                     19990623 CONTINUATION-IN-PART
            US 1999-339093
                                                                                                                        ABANDONED
            US 1997-926313
                                                      19970905 DIVISION
                                                                                                                         5968829
PRAI
            WO 1998-US18597
                                                      19980904
                                                      19991020 (Provisional)
            US 1999-160553P
            US 2004103448
                                                      20040527
FI
            US 5968829
            Utility; Patent Application - First Publication
DT
            CHEMICAL
            APPLICATION
CLMN.
              8 Figure(s).
GΙ
          FIG. 1 shows a representation of spheres of proliferating 9FBr human neural stem cells (passage 6) derived from human forebrain tissue.

FIG. 2, Panel A, shows a growth curve for a human neural stem cell line designated 6.5Fbr cultured in (a) defined media containing ***EGF***

FGF and leukemia inhibitory factor ("LIF") (shown as closed diamonds), and (b) the same media but without LIF (shown as open diamonds); Panel B shows a growth curve for a human neural stem cell line designated 9Fbr cultured in (a) defined media containing ***EGF*** FGF and LIF
            shows a growth curve for a human neural stem cell line designated 9Fbr cultured in (a) defined media containing ***EGF*** , FGF and LIF (shown as closed diamonds), and (b) the same media but without LIF (shown as open diamonds); Panel C shows a growth curve for a human neural stem cell line designated 9.5Fbr cultured in (a) defined media containing ***EGF*** , FGF and LIF (shown as closed diamonds), and (b) the same media but without LIF (shown as open diamonds); Panel D shows a growth curve for a human neural stem cell line designated 10.5Fbr cultured in (a) defined media containing ***EGF*** , FGF and leukemia inhibitory factor ("LIF") (shown as closed diamonds), and (b) the same media but
            factor ("LIF") (shown as closed diamonds), and (b) the same media but
            without LIF (shown as open diamonds).
          FIG. 3 shows a growth curve for a human neural stem cell line designated 9Fbr cultured in (a) defined media containing ***EGF*** and basic fibroblast growth factor (" ***bFGF*** ") (shown as open diamonds), and (b) defined media with ***EGF*** but without ***bFGF*** (shown as
            closed diamonds).
          FIG. 4 shows a graph of cell number versus days in culture for a Mx-1
            conditionally immortalized human glioblast line derived from a human neural stem cell line. The open squares denote growth in the presence of
            interferon; the closed diamonds denote growth in the absence of
            interferon.
          FIG. 5 shows images of rat brain after transplantation of progenitor
            cells. All transplanted cells are identified by the antigen M2 (red). Panels A-C show low power images the medial striatum labeled with M2
            (red) and BrdU (green), from A) the contralateral side of an ***EGF***
-infused animal, B) the transplant core of a vehicle-infused animal and
C) the transplant core of an ***EGF***
-infused animal. (LV=lateral
            ventricle). Panels D-G indicate co-labeling with M2 (red),
                                                                                                                                         ***GFAP***
                                                                                                                           ***EGF***
             (green) and BrdU (blue) of D) vehicle-infused, E-G)
                                                                                                                                                   -infused
            animal, with F) high power within the transplant core and G) high power within the region between the transplant and lateral ventricle.

Arrowheads indicate double-labeled BrdU/M2 cells and arrows indicate double-labeled BrdU/ ***GFAP*** cells. Panels H-K show double labeling with M2 (red) and virial (VIM; green) of H), vehicle-infused and I-K)
            ***EGF*** -infused with J) high power of the region between transplant core and lateral ventricle and K) increased expression of VIM in the SVZ. Panel L shows triple labeling with M2 (red), ***nestin*** (green),
            and BrdU (blue) of an EGFinfused animal with M) a high power image of the
            region between the transplant core and the lateral ventricle. Arrowheads indicate BrdUIM2 double-labeled cells and arrows indicate BrdU and ***nestin*** colocalization. Scale bar in M: A-C=300 mu m; D,E,H, I=40
          ***nestin*** COLOCALLZACION. The mu m; F,G,J,M=15 mu m; K,L=200 mu m.

FIG. 6 is a camera lucida drawing of a series of 1:8 coronal sections in the multiple-infused and B) ***EGF*** -infused animal showing the transplant and
            distribution of M2-positive profiles throughout the transplant and
            adjacent parenchyma. CC: corpus callosum; Str: striatum; LV: lateral
            ventricle; SM: stria medullaris. Asterisk indicates the level of cannulae
             placement and associated damage to the cortex.
          FIG. 7 shows images of the distribution of 3H-thymidine labeled cells
             (silver grains) and BrdU-labeled cells within the region between the
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and B) vehicle-infused animal. Scattered 3Hthymidine positive cells are indicated with arrows, and the occasional BrdU/3H-thymidine double-labeled cell is marked with an arrowhead (insert in A). Note the lack of 3H-thymidine labeled cells in B. Scale bar in B=80 mu m FIG. 8 shows images of beta-galactosidase (beta gal) labeling of a typical transplant. A) Within the transplant core, only immature beta gal-positive cells were observed. B and C) Occasional cells were found scattered within the striatum (B) or corpus callosum (C) and had the identity of immature oligodendrocytes. T: transplant; Ctx: cortex; CC: corpus callosum; Str: striatum. Scale bar in A=50 cm; and C (for B and C) =  $\bar{2}0$  mu m. ANSWER 5 OF 313 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 5 IFIPAT; IFIUDB; IFICDB 10584788 METHOD OF PROLIFERATING AND INDUCING BRAIN STEM CELLS TO DIFFERENTIATE TO Alvarez-Buylla Arturo; Dahmane Nadia (FR); Lim Daniel A; Palma Veronica; Ruiz I Altaba Ariel Unassigned Or Assigned To Individual (68000) 20040513 US 2004092010 A1 20030415 US 2003-414267 US 2002-372508P 20020415 (Provisional)
US 2004092010 20040513
Utility; Patent Application - First Publication CHEMICÂL APPLICATION 12 Figure(s). FIGS. 1A-1G show the localization of Gli1 and Shh gene expression in the adult SVZ. FIGS. 1A, 1D, and 1F, show that the expression of Shh mRNA is detected in the lateral wall of the lateral ventricles (LV; FIGS. 1A-1B). At higher magnifications, Shh expression is detected in SVZ cells (FIG. 1F). Arrows point to sites of expression unless otherwise noted. Ep: ependyma. FIGS. 1B, 1E, and 1G show the expression of Glil mRNA in the lateral wall of the lateral ventricle. Arrows point to sites of expression. At higher magnification, Glil expression is mostly detected in deep SVZ cells. FIG. 1C shows the control section which demonstrates the lack of hybridization with Shh antisense RNA probes in the 4th ventricle (4V). All of the in situ hybridizations shown in FIGS. 1A-1G are on cross sections. In all cases dorsal is to the top. FIGS. 2A-2B show the analyses of gene expression in sorted SVZ cells. FIG. 2A is the RT-PCR analyses of postnatal and adult cells. Postnatal whole SVZ is also shown here as control. FIG. 2B is the RT-PCR analyses of Shh expression in the SVZ and adjacent striatum from the same animal. Note that Shh is expressed in the adult SVZ but is not detected in either B or E sorted cells (FIG. 2A; see also Example 1 below). Analyses were carried out with (+) and without (-) reverse transcriptase to test for contaminating genomic DNA.

FIGS. 3A-3E show that SHH controls proliferation and neurogenesis in the SVZ. FIG. 3A shows the quantification of the effects of SHH on the proliferation of dissociated P5 SVZ cells plated on an astrocytic monolayer. BrdU incorporation was quantified by immunofluorescence. FIG. 3B shows the quantification of the effects of blocking anti-SHH monoclonal antibody (5E1) on the proliferation of P5 SVZ cells after dissociation and re-aggregation. Cell proliferation was measured by radioactive thymidine incorporation. FIG. 3C shows the quantification of the effect of SHH on neurogenesis in dissociated adult SVZ cells plated on an astrocytic monolayer. Generation of new neurons was measured by co-labeling with Tuj1, identifying neurons, and anti-BrdU antibodies, identifying cells that replicated after BrdU addition. Measurements were done after three or seven days in vitro (DIV) done after three or seven days in vitro (DIV). FIGS. 4A-4E show the models for the action of SHH on SVZ lineages. FIG. 4A shows the proposed lineage of SVZ cells from stem cells (B cells) to transiently amplifying cells (C cells) that give rise to migrating neuroblasts (A) (from Doetsch et al., Cell 97:703-716 (1999)). FIG. 4B shows that SHH acts on stem cells inducing symmetrical divisions of B cells, which transiently accumulate and then give rise C and A cells. FIG. 4 shows that SHH acts on stem cells to increase number of symmetrical divisions and/or rate of B to C transition, which then give rise to A cells. FIG. 4D shows that SHH acts on stem cells inducing symmetrical, non-renewing divisions of C cells, which amplify and then give rise to A cells. FIG. 4E shows that SHH acts on transiently amplifying C cells to increase their number or to accelerate the production of A cells.

FIG. 5 shows the morphology and gene expression in the brains of Gli2 null

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dissected brains at E18.5. Anterior is to the top. (B, C) Comparison of lateral views of dissected cortex, and dorsal views of tectum and cerebellum in wild type (B) versus Gli2-/-(C) brains. Arrows point to the posterior cortex, tectum and cerebellum. D) Comparison of wild type and
       Gli2-/cortices seen in parietal sagittal sections stained for hematoxilyn
    Gli2-/cortices seen in parietal sagittal sections stained for hematoxilyn and eosin. E-I) BrdU incorporation in wild type (E, H) and in mutant (F, I) cortices, and quantification of cell proliferation (G). Shown is the mean number of BrdU+ cells per section+-SEM from wild type and Gli2-/-animals. For simplicity, the vz was considered as the zone in between the ventricle and 5 cell diameters away, and the svz as that in between 5 and 10 cell diameters from the ventricle. P<0.05 comparing svz cells and P<0.01 for vz cell comparison. Note in (I) the uneven distribution of BrdU+ nuclei representing some variability in the thickness of the vz/svz. (J, K) Comparison of BrdU labeling in cerebellum of wild type (J) versus Gli2-/-in El8.5 samples (K). (L-Y) Images of in situ hybridization analyses of sagittal (L-U) hemisections from El8.5 and coronal sections from El5.5 (V-Y) of wild type and Gli2-/-animals probed with Gli1 (N, O), Gli2 (P, Q), Gli3 (R, S), NeuroD (L, M, T, U) clone 224
     coronal sections from E15.5 (V-Y) of wild type and Gli2-/-animals probed with Gli1 (N, O), Gli2 (P, Q), Gli3 (R, S), NeuroD (L, M, T, U) clone 224 (V, W) or clone 53 (X, Y). Note the smaller hippocampus in (U, arrow) versus (T). (Z, ZZ) Quantification of the number of NeuroD+ (Z) and clone 53+ (ZZ) cells in the dorsal telencephalon. NeuroD+ (P<0.001) or clone 53+ (P<0.001). Cb: cerebellum; cp: cortical plate; Ctx: cortex; h: hippocampus; iz: intermediate zone; Med: medulla; St: striatum; svz: subventricular zone; Tct: tectum; vz: ventricular zone. Scale bar=800 mu m for (A), 1.3 mm for (B, C), 75 mu m for (D), 50 mu m for (E,F,H,I), 130 mu m for (J-M), 320 mu m for N-U and 300 mu m for (V-Y).
  FIG. 6 shows the behavior of precursor and neurosphere-forming stem cells in Gli2 null brains. A-D) BrdU-positive cells in explant sections of wild
    in Gli2 null brains. A-D) BrdU-positive cells in explant sections of will type (A, C) and Gli2-/-(B, D) animals left untreated (A, B) or treated with SHH (C, D). E) Quantification of cell proliferation induced by SHH treatment in wild type and Gli2-/-cortical explants. Numbers represent cells per section+-SEM, with n>10 sections of at least 3 independent explants in each condition. P<0.001 comparing Gli2-/-to wild type with or without SHH. (F) RT-PCR analysis of gene expression in untreated or SHH treated wild type versus Gli2-/parietal cortical explants at E18.5. Expression of the housekeeping gene Hprt is used as internal control. Tbr1 expression confirms the cortical identity of the explants. A heterozygote Gli2+/-sample is used to show the Neo-containing and wt alleles. G-J) Phase contrast images of representative cortical nsp cultured from wild type (G, H) and Gli2-/-(I, J) animals at E18.5. K) RT-PCR analysis of cortical nsps. Note the loss of Gli1 expression, the shift in the Gli2 mutant allele band (arrows), the reduced Gli3 expression and the induction of Ihh and to a lesser extent of Dhh in Gli2-/-cells. Hprt is shown as a control. L-O) Expression of
Gli2-/-cells. Hprt is shown as a control. L-O) Expression of

**Nestin*** in precursors (L), of TuJ1 in neurons (M), of ***GFAP**
in astrocytes (N) and of O4 in oligodendrocytes (O) in Gli2-/-nsps.
Nuclei were counterstained with DAPI. P, Q) Quantification of nsp size at:
E15.5 (P) and E18.5 (Q). The average of 20 nsp from 2 independent
experiments is shown, P<0.05 for E15.5; P<0.001 for E18.5. R, S)
Quantification of nsps obtained in cloning assays. One out of three
independent experiments is shown for E15.5. P<0.001. Scale bar=300 mu m
for (A-D), 40 mu m for (G), 75 mu m for (H-J) and 10 mu m for (L-O).
FIG. 7 shows precursor proliferation and neurosphere-forming cells in Shh
null brains. A) Morphology of wild type (left, dorsal view) and
Shh-/-(right, side view) E18.5 dissected brains. Anterior is to the top.
B-E) Comparison of wild type (B, D) and Shh-/31 (C, E) cortical nsp,
obtained at E15.5 (B, C) or E18.5 (D, E). F, G) BrdU incorporation assay
on E18.5 attached nsps. H-K) Differentiation of ***Nestin*** positive
nsp (H) into neurons (Tuj1, I), astrocytes ( ***GFAP***, J) and
oligodendrocytes (O4, K) is not impaired in Shh null cultures. L). RT-PCR
analysis of E18.5 wild type and Shh null nsp cultures. M) Quantification
of wild type versus Shh-/-E15.5 and E18.5 nsp size in a single cell
clonal dilution assay. E15.5 wild type, n=12; Shh null, n=11: E18.5 wild
       Gli2-/-cells. Hprt is shown as a control. L-O) Expression of ***Nestin*** in precursors (L), of TuJ1 in neurons (M),
        clonal dilution assay. E15.5 wild type, n=12; Shh null, n=11: E18.5 wild type, n=11; Shh null, n=14. P<0.001 for E15.5, P<0.05 for E18.5. N)
Quantification of wild type versus Shh-/-E15.5 and E18.5 nsp number.
 P<0.001. O) Quantification of the number of BrdU+cells (4 days for E15.5, 1 week for E18.5) after a 7 h pulse in wild type versus Shh-/nsp. P<0.001 for E15.5 and E18.5. Scale bar=620 mu m for (A), 90 mu m for (B,C,E), 70 mu m for (D), 45 mu m for (F,G) and 15 mu m for (H-K).

FIG. 8 shows that in vivo treatment with cyclopamine inhibits neocortical proliferation and increases the number of neurosphere-forming cells. A-E) Characteristics of psp-forming cells isolated at E17.5 from control and
         Characteristics of nsp-forming cells isolated at E17.5 from control and
         cyc treated embryos. The mean of 5 animals, processed independently, is
         shown. A) Quantification of the number of nsps formed in a cloning assay
        of primary culture and first passage cells. B) Quantification of nsp
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primary and first passage cultures. Note the difference in nsp number (for primary culture P=0.4 and for the first passage P<0.001) and size (for primary culture P=0.9 and for the first passage P<0.001) between control and cyc treated animals. C) Quantification of BrdU incorporation
    in primary cultures plated in the absence of growth factors. P<0.05. D, E) Phase contrast images of representative first passage nsp cultures
    from control (D) and in vivo cyc treated (E) animals. F) Proliferation
    response of plated nsps to different concentrations of ***EGF*** with (darker bars) or without (lighter bars) added SHH (5 nM) after 1 week. A
   (darker bars) or without (lighter bars) added SHH (5 HM) after 1 week. A 7 h pulse of BrdU was given. Shown is the total number of BrdU+ cells+-SEM per well. Comparing to no SHH and decreasing concentrations of ***EGF*** : 5 nM P<0.5; 2.5 nM P<0.001; 0.5 nM P=0.001, 0.25 nM P<0.01 and 0.05 nM P<0.001. G) Quantification of BrdU+ cells in a 24 h cell culture assay in the presence of 1 ng/ml of ***EGF*** and varying concentrations of SHH (after a 7 h BrdU pulse). Compared to no SHH: 0.1 nM P=0.61; 0.5 nM P=0.58; 1 nM P<0.5; 5 nM P=0.013 and 25 nM P=0.596. Similar results were obtained with 48 h cultures. Scale bar=60 mu m for
FIG. 9 shows localization of Glil and Shh expression in the postnatal and adult SVZ. A,C) Expression of Shh mRNA in the lateral wall of the forebrain lateral ventricle (LV) of adult mice. At higher magnification, Shh expression is detected in SVZ cells (C). B, D, F-H) Expression of Glil mRNA in the lateral wall of the lateral ventricle of adult (B,D) and
Gli1 mRNA in the lateral wall of the lateral ventricle of adult (B,D) and postnatal (P3; F-H) mice. E) Control section, showing lack of hybridization of Shh anti-sense RNA probes in tissue surrounding the 4th ventricle (4V) of an adult mouse. All panels show cross sections. Arrows point to sites of expression. Dorsal is to the top. The significance of the expression in the ventral domain of the medial wall is unclear. I) Analyses of gene expression in sorted SVZ cells. RT-PCR analyses of postnatal (P5) and adult cells. Postnatal whole SVZ is also shown as control. J) RT-PCR analyses of Shh expression in the SVZ and adjacent striatum. Shh is expressed in the adult SVZ but it is not detected in either B or E sorted cells (panel I; see text). As control, all genes tested were expressed in dissected SVZ pieces. K) RT-PCR analyses of Shh, Gli and Ptch1 gene expression in P7 SVZ nsps. As controls, gene expression, including that of hprt, were measured in P7 brain RNA were tested with (+) or without (-) reverse transcriptase. Scale bar=350 mu m for (A,B,F), 100 mu m for (G), 200 mu m for C-E) and 20 mu m for (H). FIG. 10 demonstrates that SHH regulates SVZ cell proliferation and neurogenesis. A) Quantification of the effects of SHH on the proliferation of dissociated P5 SVZ cells plated on an astrocytic monolayer as measured by BrdU incorporation (Lim et al., 2001) and analysed.
     monolayer as measured by BrdU incorporation (Lim et al., 2001). B)
     Ouantification of the effects of blocking antiSHH monoclonal antibody (5E1) on the proliferation of P5 SVZ cells after dissociation and
    reaggregation. Cell proliferation was measured by radioactive thymidine incorporation. C) Quantification of the effect of SHH on neurogenesis in dissociated adult SVZ cells plated on an astrocytic monolayer. Generation of new neurons was measured by co-labeling with Tujl, identifying neurons, and anti-BrdU antibodies. Measurements were done after 3-7 days. D) Quantification of the effects of SHH on isolated P5, type A SVZ peuroblasts. Cells were corted and grown in vitro on poly-lygine coated
     neuroblasts. Cells were sorted and grown in vitro on poly-lysine coated
    neuroblasts. Cells were sorted and grown in vitro on poly-lysine coated glass for 7 days with 10 nM SHH, passaged and cultured for 3 days and one week. Live neuroblasts were quantified by analysis of Tujl immunostaining and fluorescent nuclear counterstaining. The number of Tujlpositive cells with non-pycnotic nuclei in SHH treated cultures were counted and expressed as a percentage of control cultures performed in parallel. E) Immunocytochemistry of one week SVZ culture on an astrocytic monolayer. BrdU was added to the culture medium 24 hours prior to fixation. Shown is the labeling of neurons with TuJ1 (red) and recently divided cells with anti-BrdU (green) antibodies. Note the large number of doubly labeled (vellow) cells representing newly born cells. F) Nomarski optics images
     (yellow) cells representing newly born cells. F) Nomarski optics images of the sample panel shown in E). G, H) Postnatal SVZ cells were plated in medium with 10% FCS for 3 days, conditions allowing SVZ astrocytes to
      form a monolayer. The medium was then changed to serum-free medium, with
     or without SHH. After 4 more days, cultures were enzymatically dissociated to single cells, counted, and equal numbers of cells were plated nsp medium containing ***EGF*** (10 ng/ml). (G) 2.3fold more nsps grew from SHH treated SVZ cells as compared to control SVZ cells.
       (H) Similarly, there were 2.4-fold more nsps derived from SHH-treated SVZ
      cells after passage of nsps from cultures in (G). Scale bar=45 mu m for (E,F). In all cases, error bars show SEM of triplicate cultures.
   FIG. 11 shows that in vivo blocking HH signaling decreases SVZ
      proliferation and increases the number of neurosphere-forming stem cells. A-F) Characterization of SVZ cells of HBC-vehicle control (A, B and E)
      and cyc (C, D and F) injected adults (after 7 days n cyc treatment in
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cells. Note that whereas some cyc-treated animals do show little or no BrdU staining (C, also detail in D), there is an intrinsic variability in the response of cyc-treated animals. I) Quantification of BrdU positive
  cells per section in control (n=6) and cyc-treated (n=11) adult mice. Four out of eleven animals did not respond to cyc treatment. Without counting these, the difference is greater (white bar). E, F) Detailed
  image of the lateral walls, showing cells positively stained for ***Nestin*** (green) and ***GFAP*** (red) of control (E) and
 image of the lateral walls, showing cells positively stained for ***Nestin*** (green) and ***GFAP*** (red) of control (E) and cyctreated animals (F). G, H, J and K) Characteristics of SVZ progenitor cells isolated at P9 from control and cyc treated pups (5 days treatment in vivo starting at P4). Two independent experiments, pooling 5 animals in each case for the nsp preparation, were done. G,H) Phase contrast images of representative nsps cultured from control (G) and cyc-in vivo treated (H) animals. J,K) Number and size of nsp, obtained in cloning assays, plated as described in FIG. 4. (size: primary culture P=0.2, and first passage P<0.001; number: primary culture P<0.5 and first passage P<0.05). LV: lateral ventricle. Scale bar=230 mu m for (A,C), 50 mu m for (B,D,E,F) and 130 mu m for (G,H).
    (B,D,E,F) and 130 mu m for (G,H)
                                                                                                                                                                                  ***EGF***
FIG. 12 shows a model for the action of SHH and
   amplifying precursors and stem cells in the brain. In vivo,
  cycling stem cells (stem cell 1) give rise to transit amplifying precursors. These then give rise to committed precursors and to differentiated cells. In the SVZ this would correspond to the
 B->C->A->neuron lineage (Alvarez-Buylla et al., (2001) Nat. Rev.
Neurosci. 2:287-293). In the developing neocortex, the distinction
between stem cell and amplifying precursor is less clear. Stem cells and
amplifying precursors can give rise to nsps (red dashed box) in vitro in
the presence of ***EGF***. Amplifying precursors form the bulk of the
BrdU+ cells (green box). These can behave as stem cells (stem cell 2) and
form the bulk of nsps formed in vitro (blue) as seen with SVZ C cells
  form the bulk of nsps formed in vitro (blue), as seen with SVZ C cells (Doetsch et al., (2002) Neuron 36: 1021-1034). SHH and ***EGF*** signaling act on amplifying precursors (black arrows) which can behave as stem cells, but also possibly on slow cycling stem cells (EGFR+/Gli1+ B cells in the SVZ) (gray arrows). Brain tumors may initiate from the inappropriate expansion of cells with stem cell properties (see Peva et
  inappropriate expansion of cells with stem cell properties (see Reya et al., (2001) Nature 414:105-111; Ruiz i Altaba et al., (2002b) Nat. Rev. Cancer 2:361-372) through enhanced SHH or ***EGF*** signaling acting
                                                                                                                                                                                                         signaling acting
   on the stem cell 1 or, the amplifying precursor (stem cell 2)
   populations. !
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24 Figure(s).
FIGS. 1A-1G show the localization of Glil and Shh gene expression in the adult SVZ. FIGS. 1A, 1D, and 1F, show that the expression of Shh mRNA is detected in the lateral wall of the lateral ventricles (LV; FIGS. 1A-1B). At higher magnifications, Shh expression is detected in SVZ cells (FIG. 1F). Arrows point to sites of expression unless otherwise noted. Ep: ependyma. FIGS. 1B, 1E, and 1G show the expression of Glil mRNA in the lateral wall of the lateral ventricle. Arrows point to sites of expression. At higher magnification, Glil expression is mostly detected in deep SVZ cells. FIG. 1C shows the control section which demonstrates the lack of hybridization with Shh antisense RNA probes in the 4th ventricle (4V). All of the in situ hybridizations shown in FIGS. 1A-1G are on cross sections. In all cases dorsal is to the top.

FIGS. 2A-2B show the analyses of gene expression in sorted SVZ cells. FIG. 2A is the RT-PCR analyses of postnatal and adult cells. Postnatal whole SVZ is also shown here as control. FIG. 2B is the RT-PCR analyses of Shh expression in the SVZ and adjacent striatum from the same animal. Note

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E sorted cells (FIG. 2A; see also Example 1 below). Analyses were carried out with (+) and without (-) reverse transcriptase to test for
  contaminating genomic DNA.
FIGS. 3A-3E show that SHH controls proliferation and neurogenesis in the
  SVZ. FIG. 3A shows the quantification of the effects of SHH on the
  proliferation of dissociated P5 SVZ cells plated on an astrocytic
  monolayer. BrdU incorporation was quantified by immunofluorescence. FIG.
  3B shows the quantification of the effects of blocking anti-SHH
  monoclonal antibody (5E1) on the proliferation of P5 SVZ cells after dissociation and re-aggregation. Cell proliferation was measured by radioactive thymidine incorporation. FIG. 3C shows the quantification of the effect of SHH on neurogenesis in dissociated adult SVZ cells plated
  on an astrocytic monolayer. Generation of new neurons was measured by
  co-labeling with Tujl, identifying neurons, and anti-BrdU antibodies, identifying cells that replicated after BrdU addition. Measurements were
  done after three or seven days in vitro (DIV)
FIGS. 4A-4E show the models for the action of SHH on SVZ lineages. FIG. 4A
  shows the proposed lineage of SVZ cells from stem cells (B cells) to
  transiently amplifying cells (C cells) that give rise to migrating neuroblasts (A) (from Doetsch et al., Cell 97:703-716 (1999)). FIG. 4B shows that SHH acts on stem cells inducing symmetrical divisions of B cells, which transiently accumulate and then give rise C and A cells. FIG. 4 shows that SHH acts on stem cells to increase number of symmetrical divisions and/or rate of B to C transition, which then give
  rise to A cells. FIG. 4D shows that SHH acts on stem cells inducing
  symmetrical, non-renewing divisions of C cells, which amplify and then give rise to A cells. FIG. 4E shows that SHH acts on transiently
  amplifying C cells to increase their number or to accelerate the
  production of A cells.
FIG. 5 shows the morphology and gene expression in the brains of Gli2 null animals. (A) Dorsal morphology of wild type (left) and Gli2-/-(right) dissected brains at E18.5. Anterior is to the top. (B, C) Comparison of lateral views of dissected cortex, and dorsal views of tectum and
  cerebellum in wild type (B) versus Gli2-/-(C) brains. Arrows point to the
  cerebellum in wild type (B) versus G112-/-(C) brains. Arrows point to the posterior cortex, tectum and cerebellum. D) Comparison of wild type and G1i2-/cortices seen in parietal sagittal sections stained for hematoxilyn and eosin. E-I) BrdU incorporation in wild type (E, H) and in mutant (F, I) cortices, and quantification of cell proliferation (G). Shown is the mean number of BrdU+ cells per section +-SEM from wild type and G1i2-/-animals. For simplicity, the vz was considered as the zone in between the ventricle and *5 cell diameters away, and the svz as that in between *5 and *10 cell diameters from the ventricle. P less-than 0.05
  between *5 and *10 cell diameters from the ventricle. P less-than 0.05
   comparing svz cells and P less-than 0.01 for vz cell comparison.
  comparing svz cells and P less-than 0.01 for vz cell comparison. Note in (I) the uneven distribution of BrdU+ nuclei representing some variability in the thickness of the vz/svz. (J, K) Comparison of BrdU labeling in cerebellum of wild type (J) versus Gli2-/-in E18.5 samples (K). (L-Y) Images of in situ hybridization analyses of sagittal (L-U) hemisections from E18.5 and coronal sections from E15.5 (V-Y) of wild type and Gli2-/-animals probed with Gli1 (N, O), Gli2 (P, Q), Gli3 (R, S), NeuroD (L, M, T, U) clone 224 (V, W) or clone 53 (X, Y). Note the smaller hippocampus in (U, arrow) versus (T). (Z, ZZ) Quantification of the number of NeuroD+ (Z) and clone 53+ (ZZ) cells in the dorsal telencephalon. NeuroD+ (P less-than 0.001) or clone 53+ (P less-than 0.001). Cb: cerebellum: cp: cortical plate; Ctx: cortex; h: hippocampus;
  0.001). Cb: cerebellum; cp: cortical plate; Ctx: cortex; h: hippocampus; iz: intermediate zone; Med: medulla; St: striatum; svz: subventricular zone; Tct: tectum; vz: ventricular zone. Scale bar=800 mu m for (A), 1.3 mm for (B, C), 75 mu m for (D), 50 mu m for (E,F,H,I), 130 mu m for (J-M), 320 mu m for N-U and 300 mu m for (V-Y).
FIG. 6 shows the behavior of precursor and neurosphere-forming stem cells
  FIG. 6 shows the behavior of precursor and neurosphere-forming stem cells in Gli2 null brains. A-D) BrdU-positive cells in explant sections of wild type (A, C) and Gli2-/-(B, D) animals left untreated (A, B) or treated with SHH (C, D). E) Quantification of cell proliferation induced by SHH treatment in wild type and Gli2-/-cortical explants. Numbers represent cells per section +-SEM, with n greater-than 10 sections of at least 3 independent explants in each condition. P less-than 0. 001 comparing Gli2-/-to wild type with or without SHH. (F) RTPCR analysis of gene expression in untreated or SHH treated wild type versus Gli2-/-parietal cortical explants at E18.5. Expression of the housekeeping gene Hprt is used as internal control. Tbr1 expression confirms the cortical identity of the explants. A heterozygote Gli2+/-sample is used to show the
   of the explants. A heterozygote Gli2+/-sample is used to show the
   Neocontaining and wt alleles. G-J) Phase contrast images of
  representative cortical nsp cultured from wild type (G, H) and Gli2-/-(I, J) animals at E18.5. K) RT-PCR analysis of cortical nsps. Note the loss of Gli1 expression, the shift in the Gli2 mutant allele band (arrows), the reduced Gli3 expression and the induction of Ihh and to a lesser
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of ***Nestin*** in precursors (L), of TuJ1 in neurons (M), of ***GFAP*** in astrocytes (N) and of O4 in oligodendrocytes (O) in Gli2-/-nsps. Nuclei were counterstained with DAPI. P, Q) Quantification of nsp size at E15.5 (P) and E18.5 (Q). The average of 20 nsp from 2 independent experiments is shown P less-than 0.05 for E15.5; P less-than
    0.001 for E18.5. R, S) Quantification of nsps obtained in cloning assays.
    One out of three independent experiments is shown for E15.5. P less-than
    0.001. Scale bar=300 mu m for (A-D), 40 mu m for (G), 75 mu m for (H-J)
    and 10 mu m for (L-0).
FIG. 7 shows precursor proliferation and neurosphere-forming cells in Shh
  null brains. A) Morphology of wild type (left, dorsal view) and Shh-/-(right, side view) E18.5 dissected brains. Anterior is to the top. B-E) Comparison of wild type (B, D) and Shh-/-(C, E) cortical nsp, obtained at E15.5 (B, C) or E18.5 (D, E). F, G) BrdU incorporation assay on E18.5 attached nsps. H-K) Differentiation of ***Nestin*** positive nsp (H) into neurons (Tuj1, I), astrocytes ( ***GFAP*** , J) and oligodendrocytes (O4, K) is not impaired in Shh null cultures. L). RT-PCR analysis of E18.5 wild type and Shh null nsp cultures. M) Quantification of wild type versus Shh-/-F15 5 and E18.5 nsp size in a single cell
  analysis of E18.5 wild type and Shh null hsp cultures. M) Quantification of wild type versus Shh-/-E15.5 and E18.5 nsp size in a single cell clonal dilution assay. E15.5 wild type, n=12; Shh null, n=11: E18.5 wild type, n=11; Shh null, n=14. P less-than 0.001 for E15.5, P less-than 0.05 for E18.5. N) Quantification of wild type versus Shh-/-E15.5 and E18.5 nsp number. P less-than 0.001. O) Quantification of the number of BrdU+cells (4 days for E15.5, 1 week for E18.5) after a 7h pulse in wild type versus Shh-/-nsp. P less-than 0.001 for E15. 5 and E18.5. Scale bar=620 mu m for (A) 90 mu m for (B C E) 70 mu m for (D) 45 mu m for (F G) and
    mu m for (A), 90 mu m for (B,C,E), 70 mu m for (D), 45 mu m for (F,G) and 15 mu m for (H-K).
FIG. 8 shows that in vivo treatment with cyclopamine inhibits neocortical proliferation and increases the number of neurosphere-forming cells. A-E) Characteristics of nsp-forming cells isolated at E17.5 from control and cyc treated embryos. The mean of 5 animals, processed independently, is shown. A) Quantification of the number of nsps formed in a cloning assay
    of primary culture and first passage cells. B) Quantification of nsp size. A minimum of n=10 nsp were selected to measure the nsp diameter of
   primary and first passage cultures. Note the difference in nsp number (for primary culture P=0.4 and for the first passage P less-than 0.001) and size (for primary culture P=0.9 and for the first passage P less-than 0.001) between control and cyc treated animals. C) Quantification of BrdU incorporation in primary cultures plated in the absence of growth factors. P less-than 0.05. D, E) Phase contrast images of representative first passage nsp cultures from control (D) and in vivo cyc treated (E) animals. F) Proliferation response of plated pages to different
    animals. F) Proliferation response of plated nsps to different concentrations of ***EGF*** with (darker bars) or without (lighter
   concentrations of ***EGF*** with (darker bars) or without (lighter bars) added SHH (5 nM) after 1 week. A 7 h pulse of BrdU was given. Shown is the total number of BrdU+ cells +-SEM per well. Comparing to no SHH and decreasing concentrations of ***EGF***: 5 nM P less-than 0.5; 2.5 nM P less-than 0.001; 0.5 nM P=0.001, 0.25 nM P less-than 0.01 and 0.05 nM P less-than 0.001. G) Quantification of BrdU+ cells in a 24 h cell culture assay in the presence of 1 ng/ml of ***EGF*** and varying concentrations of SHH (after a 7 h BrdU pulse). Compared to no SHH: 0.1 nM P=0.61; 0.5 nM P=0.58; 1 nM P lessthan 0.5; 5 nM P=0.013 and 25 nM P=0.596. Similar results were obtained with 48 h cultures. Scale bar=60 mu m for (D E)
    mu m for (D,E).
FIG. 9 shows localization of Gli1 and Shh expression in the postnatal and
   adult SVZ. A,C) Expression of Shh mRNA in the lateral wall of the forebrain lateral ventricle (LV) of adult mice. At higher magnification, Shh expression is detected in SVZ cells (C). B, D, F-H) Expression of Gli1 mRNA in the lateral wall of the lateral ventricle of adult (B,D) and postnatal (P3; F-H) mice. E) Control section, showing lack of
    hybridization of Shh anti-sense RNA probes in tissue surrounding the 4th
    ventricle (4V) of an adult mouse. All panels show cross sections. Arrows point to sites of expression. Dorsal is to the top. The significance of
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Analyses of gene expression in sorted SVZ cells. RT-PCR analyses of
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tested were expressed in dissected SVZ pieces. K) RT-PCR analyses of Shh,
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expression, including that of hprt, were measured in P7 brain RNA were
tested with (+) or without (-) reverse transcriptase. Scale bar=350 mu m
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    neurogenesis. A) Quantification of the effects of SHH on the
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   neurons, and anti-BrdU antibodies. Measurements were done after 3-7 days.
  D) Quantification of the effects of SHH on isolated P5, type A SVZ neuroblasts. Cells were sorted and grown in vitro on poly-lysine coated glass for 7 days with 10 nM SHH, passaged and cultured for 3 days and one week. Live neuroblasts were quantified by analysis of Tujl immunostaining and fluorescent nuclear counterstaining. The number of Tujlpositive cells with non-pycnotic nuclei in SHH treated cultures were counted and expressed as a percentage of control cultures performed in parallel F)
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   Immunocytochemistry of one week SVZ culture on an astrocytic monolayer.
   BrdU was added to the culture medium 24 hours prior to fixation. Shown is
  the labeling of neurons with TuJ1 (red) and recently divided cells with anti-BrdU (green) antibodies. Note the large number of doubly labeled (yellow) cells representing newly born cells. F) Nomarski optics images of the sample panel shown in E). G, H) Postnatal SVZ cells were plated in medium with 10% FCS for 3 days, conditions allowing SVZ astrocytes to form a monolayer. The medium was then changed to serum-free medium, with
   or without SHH. After 4 more days, cultures were enzymatically
   dissociated to single cells, counted, and equal numbers of cells were plated nsp medium containing ***EGF*** (10 ng/ml). (G) 2.3fold mo
   plated nsp medium containing
                                                                                                                                 (10 ng/ml). (G) 2.3fold more
   nsps grew from SHH treated SVZ cells as compared to control SVZ cells.
(H) Similarly, there were 2.4-fold more nsps derived from SHH-treated SVZ cells after passage of nsps from cultures in (G). Scale bar=45 mu m for (E,F). In all cases, error bars show SEM of triplicate cultures.

FIG. 11 shows that in vivo blocking HH signaling decreases SVZ proliferation and increases the number of neurosphere-forming stem cells.

A-F) Characterization of SVZ cells of HBC-vehicle control (A, B and E)
   and cyc (C, D and F) injected adults (after 7 days n cyc treatment in vivo). A,C) BrdU staining after a 2 h pulse). Arrows denote BrdU positive
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  ***Nestin*** (green) and ***GFAP*** (red) of control (E) and cyctreated animals (F). G, H, J and K) Characteristics of SVZ progenitor cells isolated at P9 from control and cyc treated pups (5 days treatment in vivo starting at P4). Two independent experiments, pooling 5 animals in each case for the nsp preparation, were done. G,H) Phase contrast images of representative nsps cultured from control (G) and cyc-in vivo treated (H) animals. J,K) Number and size of nsp, obtained in cloning assays, plated as described in FIG. 4. (size: primary culture P=0.2, and first passage P less-than 0 001: number: primary culture P less-than 0.5
   first passage P less-than 0.001; number: primary culture P less-than 0.5 and first passage P less-than 0.05). LV: lateral ventricle. Scale
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  amplifying precursors and stem cells in the brain. In vivo, slow cycling stem cells (stem cell 1) give rise to transit amplifying precursors. These then give rise to committed precursors and to
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   Stem cells and amplifying precursors can give rise to nsps (red dashed box) in vitro in the presence of ***EGF*** . Amplifying precursors
 Stem cells and amplifying precursors can give rise to nsps (red dashed box) in vitro in the presence of ***EGF*** . Amplifying precursors form the bulk of the BrdU+ cells (green box). These can behave as stem cells (stem cell 2) and form the bulk of nsps formed in vitro (blue), as seen with SVZ C cells (Doetsch et al., (2002) Neuron 36: 1021-1034). SHH and ***EGF*** signaling act on amplifying precursors (black arrows) which can behave as stem cells, but also possibly on slow cycling stem cells (EGFR+/ Gli1+ B cells in the SVZ) (gray arrows). Brain tumors may initiate from the inappropriate expansion of cells with stem cell properties (see Reya et al., (2001) Nature 414:105-111; Ruiz i Altaba et al., (2002b) Nat. Rev. Cancer 2:361-372) through enhanced SHH or ***EGF*** signaling acting on the stem cell 1 or, the amplifying
   ***EGF*** signaling acting on the stem cell 1 or, the amplifying precursor (stem cell 2) populations.
FIG. 13 Model for the action of Shh in the dorsal brain
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blocking its activity
       FIG. 15 Demonstration that GLI genes are consistently expressed in primary
         brain tumors
                16 Demonstration that Cyclopamine, a drug that inhibits the response
         to Shh signaling modulates the proliferation of a subset of brain tumor
         cell lines
       FIG. 17 Effect of cyclopamine in a long-term treatment of a glioblastoma
         cell line (U87) in vitro. Shh-Gli pathway controls proliferation and
       FIG. 18 Cyclopamine modulates the proliferation of primary cortical gliomas that were dissociated and cultured in vitro
FIG. 19 Demonstration that only a subset of cells from primary brain tumors, dissociated and cultured in vitro, have stem-like properties, and their proliferation is inhibited by the presence of cyclopamine
FIG. 20 In vivo cyclopamine treatment reduces the size of medulloblastomas of Ptch+/-, p53-/-mice
FIG. 21 Percentage of BrdU incorporation in the presence or absence of 5
         viability of brain tumor cells
        FIG. 21 Percentage of BrdU incorporation in the presence or absence of 5
         mu m cyclopamine
        FIG. 22 siRNAs for Gli1 and Gli2 block Shh responses in 10T1/2 cells
        FIG. 23 Downregulation of Gli1 and Gli2 inhibits U87 glioma cell
         proliferation
        FIG. 24 Proliferation of primary brain tumor cells is inhibited by
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         LOW OXYGEN CULTURING OF CENTRAL NERVOUS SYSTEM PROGENITOR CELLS
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California Institute of Technology
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                                            19981118 CONTINUATION-IN-PART
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          Utility; Patent Application - First Publication
          CHEMICAL
          APPLICATION
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          62
           8 Figure(s).
        FIG. 1. Effect of lowered oxygen on precursor yield in vitro at varying
         plating densities. Striatal cultures were expanded with ***bFGF*** in lowered or ambient oxygen, and total cell numbers assessed after 5 days of proliferation when over 95% of cells are ***nestin*** + precursors. Significantly increased cell numbers were detected at all densities in
          lowered O2 compared to ambient oxygen.
        FIG. 2. Lowered oxygen culturing leads to increased proliferation of CNS precursors. FIG. 2A. Mesencephalic precursors were pulsed with 10 mu M BrdU for 60 minutes immediately before fixation, then stained for BrdU
          uptake. More BrdU+ cells were seen in lowered oxygen cultures during both
          proliferation and differentiation. Scale bar=20 mu m. FIG. 2B.
          Mesencephalic precursors in lowered O2 yielded an increased percentage of
          BrdU+ cells and a greater absolute number of BrdU+ cells than cultures maintained at 20% O2. Data are given as mean+/-SEM, n=40. Differences between lowered and 20% O2 were statistically significant at all time
        points and for all parameters (n=8, p less-than 0.05) except percentage of BrdU+ cells at day 4 of expansion (n=8, p=0.10). FIG. 3. CNS precursors cultured in lowered (vs. 20%) O2 have reduced rates
          of apoptosis. FIG. 3A. Apoptosis was assayed by TUNEL labeling of mesencephalic precursors cultured in parallel at either lowered or 20% O2 Representative figures of the expansion phase (2 and 6 days of culture) and the differentiation phase (4 days after ***bFGF*** withdrawal)
          and the differentiation phase (4 days after ***bFGF*** withdrawal) are shown. Scale bar=20 mu m. FIG. 3B. Precursors grown at lowered 2. showed a significant decrease in the percentage of apoptotic cells (n=8, p less-than 0.05) compared to traditional cultures.
        FIG. 4. Basic differentiation patterns of CNS stems in lowered and 20% O2 cultures. FIG. 4A. Striatal cultures in lowered or 20% O2 were assessed
          for the relative percentages of precursorderived neurons (by TUJ1 stain), astrocytes ( ***GFAP*** ) and oligodendrocytes (Gal-C) after 5 days of
          astrocytes (
           ***bFGF*** proliferation followed by four days of cell differentiation (for quantification see text). FIG. 4B. Passaged mesencephalic precursors
          were proliferated for 6 days and differentiated for 5 days in lowered or
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cells could be detected only in lowered oxygen cultures. FIG. 4C. \*\*\*Nestin\*\*\* + clones were derived from single passaged mesencephalic precursor cells after 20 days of \*\*\*bFGF\*\*\* proliferation (left panel). Clones in lowered oxygen differentiated into TUJ1+ neurons upon panel). Clones in lowered oxygen differentiated into TUJ1+ neurons upon \*\*\*bFGF\*\*\* withdrawal (right panel). FIG. 4D. Lowered O2 promotes clor formation efficiency. The yield of clones derived from single precursors was 3-fold higher in lowered O2 compared to 20% O2 cultures (left panel). The majority of clones derived from precursors in O2 oxygen cultures contained 50-500 cells whereas clone size in 20% O2 cultures was generally 5-50 cells (right panel). Scale bar=20 mu m in all panels. FIG. 5. Lowered O2 culturing improves the yield of functional precursor-derived dopaminergic neurons. FIG. 5A and FIG. 5B. Precursors from E12 mesencephalon were proliferated with \*\*\*bFGF\*\*\* for 5 days from E12 mesencephalon were proliferated with \*\*\*bFGF\*\*\* for 5 days followed by 5 days of differentiation, then stained for the neuronal marker TUJ1 and for TH. A large increase in total number (and percentage) marker TUJî and for TH. A large increase in total number (and percentage) of TH+ neurons was detected (p less-than 0.001) in lowered 02 compared to 20% 02 cultures. Scale bar=20 mu m. FIG. 5C. Quantification of TH protein level by Western blot analysis revealed significantly more TH in samples from lowered (vs. 20%) 02 cultures. Each lane was loaded with 2.5 m mu g total protein. FIG. 5D. rp-HPLC with electrochemical detection was used to quantify dopamine levels in conditioned medium (24 hrs), in HBSS after 15 minutes of conditioning (basal release), and in HBSS+56 mM KCl after 15 minutes (evoked release). Significantly more dopamine was detected in cultures maintained at lowered 02 compared to those grown at 20% 02 under all these conditions (conditioned medium p less-than 0.01; basal and evoked release p less-than 0.05). Inset shows typical chromatogram for evoked release p less-than 0.05). Inset shows typical chromatogram for dopamine detection in lowered and 20% 02 cultures.

FIG. 6. Neuronal subtype differentiation from mesencephalic precursors in levered we 20% 02 perhaps and 20% of the contract of the lowered vs. 20% O2. Double immunocytochemical labeling revealed that lowered O2 culturing markedly increased the representation of dopaminergic and serotonergic neuronal (Tujl+) subtypes, but decreased the representation of GABA+ and Glutamate+ neurons. Colony depicted in GABA stain at 20% O2 is an unusual example of very high GABA expression under these conditions. TH and GABA were not co-expressed as seen in some developing neurons in vivo. Floor plate cells (FP4+) were more numerous in lowered O2 cultures as was the percentage of neurons expressing the midbrain transcription factor En1. Precursor markers \*\*\*nestin\*\*\* at PSA-NCAM were both reduced in lowered O2 cultures after differentiation compared to 20% O2 conditions (lower right panels). Scale bars=20 mu m. FIG. 7. Differential gene expression in mesencephalic precursors at lowered and 20% O2 assessed by PT-DCP FIG. 73 Expression of genes lowered and 20% O2 assessed by RT-PCR. FIG. 7A. Expression of genes involved in the physiological response to changes in oxygen levels. The expression of HIF1 alpha, VHL, EPO and VEGF was assessed after 2 or 6 days of expansion and after differentiation (day 4 of differentiation=day 10 of culture) in lowered and 20% O2. Data are normalized to GAPDH expression. A significant increase in EPO expression was detected in lowered oxygen versus 20% O2 mostly during cell differentiation, whereas VEGF was upregulated during both expansion and differentiation. Surprisingly, no major oxygen-dependent regulation of HIF1 alpha or VHI. Surprisingly, no major oxygen-dependent regulation of HIF1 alpha or VHL was observed. FIG. 7B. Candidate genes involved in midbrain development were also tested for O2-dependent differential expression. Increased expression of TH and Ptx-3 during cell differentiation confirmed the expression of TH and Ptx-3 during cell differentiation confirmed the larger number of functional dopaminergic neurons in lowered oxygen cultures (compare FIG. 5). Significant lowered O2-mediated changes in expression levels of FGF8 and En1 were also detected.

FIG. 8. EPO mimics the lowered oxygen effect on dopaminergic differentiation. Saturating concentrations of EPO or EPO neutralizing antibody were added to E12 mesencephalic precursor cultures during both proliferation and differentiation phase (5 days each) in lowered or 20% O2. EPO supplementation significantly increased TH+ cell numbers in 20% O2 cultures (n=6, p less-than 0.05). EPO neutralizing antibody decreased TH+ cell numbers in both lowered oxygen (n=6, p less-than 0.01) and 20% O2 cultures (n=6, p less-than 0.05). Scale bar=20 mu m. 02 cultures (n=6, p less-than 0.05). Scale bar=20 mu m.

ANSWER 8 OF 313 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 8

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ENGRAFTABLE HUMAN NEURAL STEM CELLS; PRIMORDIAL HUMAN NEURAL STEM CELL
CLONE COMPRISING BOTH EPIDERMAL- AND FIBROBLAST GROWTH FACTOR RECEPTORS;
GENE EXPRESSION, GENETIC ENGINEERING AND CELLULAR DIFFERENTIATION
IN Kim Seung U (CA); Snyder Evan Y; Wolfe John H
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PA British Columbia, University of CA Children's Medical Center Corp The Pennsylvania, University of (10709, 11738, 64664)
PI US 6680198 B1 20040120

19980814 CONTINUATION 5958767

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US 5958767 Utility; Granted Patent - Utility, no Pre-Grant Publication

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9 Drawing Sheet(s), 53 Figure(s).
FIGS. 1A and 1B: The monoclonal nature of each putative human neural stem cell (NSC) clone is confirmed by demonstrating a single retroviral insertion site within the genomic DNA from the \*\*\*bFGF\*\*\* putative human NSC clone HI (which was propagated in subsequently transduced with a retrovirus encoding lacZ and neo) was digested with Hind III (which cuts only once within the provirus) and incubated with a radiolabeled nucleotide probe complementary to neo.

Monoclonal derivation is confirmed by the presence of a single integrated retrovirus with an integration site common to all cells in the colony indicating that they were derived from a single infected "parent" cell (arrow). As a positive control, the murine NSC clone C17.2 which contains 2 integrated retroviruses encoding neo (one from an integrated vmyc-encoding retrovirus and one from a separate lacZ-encoding retrovirus13,28 appropriately shows 2 bands (arrows). Specificity of the retrovirus 13,28 appropriately snows 2 bands (arrows). Specificity of the probe is demonstrated by the negative control, the human meduloblastoma cell line DaOY, which, having not been infected with a retrovirus, shows no neo sequences in its genome and hence no hybridization product (B) Genomic DNA from putative clones H9, H6, D10, and C2 (human NSC colonies propagated in \*\*\*bFGF\*\*\* and/or \*\*\*EGF\*\*\* and then subsequently infected with a retrovirus encoding the propagating gene vmyc) were digested with Bgl II or Bam HI (each of which cuts only once within the provirus) and then subjected to Southern analysis utilizing a probe provirus) and then subjected to Southern analysis utilizing a probe complementary to the proviral vmyc. Single retroviral integration sites are appreciated in all colonies confirming the monoclonal nature of each putative clone. The murine NSC clone C17.2, which contains a single copy of vmyc13,28 and serves as a positive control, also has one band. As in (A), the negative control non-virally infected human DaOY cells, have no bands. 2A-2E: Characterization of human neural stem cells (NSCs) in vitro. (A) NSCs tend to grow as clusters in serum-free bFGFsupplemented medium. They differentiate spontaneously into neurofilament-immunoreactive neurons (B) or CNPaseimmunoreactive oligodendrocytes (C) when transferred to serumcontaining medium, or into \*\*\*GFAP\*\*\* -expressing astrocytes when cocultured with primary murine CNS cultures (and identified with a human-specific anti- \*\*\*GFAP\*\*\* antibody) as, for example in (D), illustrating a typical type-1 protoplasmic astrocyte. Hence, a single clone has the potential for generating cella of all neural lineages ("multipotency"). New immature, undifferentiated, vimentin-immunoreactive NSCs (E) are present in clones under all conditions, suggesting the ability of a clone to "self-renew" (i.e., produce new multipotent NSCs). FIGS. 3A-3N: Human neural stem cells (NSCs) are capable of complementing a prototypical gene product deficiency (e.g., beta-hexosaminidase-A) in neural cells of multiple lineages in which the gene is mutated (e.g., brain cells from Tay-Sachs mice). As a proof of principle that human NSCs (like murine NSCs) are capable of cross-correcting a neurogenetic defect, neural cells from the brains of mice with the prototypical neurogenetic disorder Tay-Sachs disease, generated via targeted mutagenesis of the They differentiate spontaneously into neurofilament-immunoreactive disorder Tay-Sachs disease, generated via targeted mutagenesis of the alpha-subunit of beta-hexosaminidase resulting in absence of hexosaminidase-A39, were exposed to secreted gene products from human NSCs to assess their ability to effect complementation of the defect. (A-C) Hexosaminidase activity as determined by NASBG histochemistry (Nomarski optics). Functional hexosaminidase produces a red-pink precipitate with an intensity proportional to the level of activity. (A) Tay-Sachs neural cells (arrows) not exposed to NSCs have no, or minimal, detectable hexosaminidase. (A small number of faintly pink NASBG+ cells are occasionally observed reflecting low residual hexosaminidase-B activity). In comparison, Tay-Sachs neural cells exposed to secretory products from murine NSCs (e.g., clone C17.2H) (B) or from human NSCs (C) now stain intensely red (wildtype intensity) suggesting that they have been cross-corrected, i.e., have internalized significant amounts of functionally active hexosaminidase from the NSCconditioned medium. (D-L) To help determine which neural cell types from the Tay-Sachs brain were cross-corrected, primary dissociated Tay-Sachs neural cells which had been co-cultured in a transwell system with human NSCs (as in (C)) were reacted both with a fluorescein-labeled antibody to the human alphasubunit of hexosaminidase (D-F) and with antibodies to neural cell type-specific antigens (visualized by a TR-tagged secondary antibody)

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co-localization of the alphasubunit with the cell-type markers (J-L,
  respectively). A subset of these now alpha-subunit-positive corrected
  cells (D) were neurons, as indicated by their expression of the neuronal
  marker NeuN (G,J); a subset of the alpha-subunit+ cells (E) were glial,
  as illustrated by their co-expression of the glial marker ***GFAF (H,K); and a subset of the alpha-subunit+ cells (F) were immature.
                                                                                                                                                           ***GFĂP***
  undifferentiated CNS precursors, as indicated by the presence of the intermediate filament ***nestin*** (I,L). (Untreated cells from
                                                                                                    (I,L). (Untreated cells from a
 Tay-Sachs brain do not stain for the alpha-subunit). (M) Percentage of successfully rescued (i.e., NASBG+) primary Tay-Sachs neural cells as seen in (A-C). The number of "untreated" Tay-Sachs alpha-subunit-null cells (-/-) (i.e., unexposed to NSCs) that were NASBG+ (1st histogram) was quite low. (That the percentage is not 0 reflects some low residual hexosaminidase-B activity in mutant cells that is sometimes sufficient apough in some cells to produce a pale pink scoreable cell). In contrast
  enough in some cells to produce a pale pink scoreable cell). In contrast, among Tay-Sachs neural cells "treated" with secretory products from
  murine NSCs (C17.2) (2nd histogram), murine NSCs engineered to over-express hexosaminidase (C17.2H) (3rd histogram), or human NSCs (4th
 histogram), the percentage of cross-corrected, hexosaminidasecontaining cells was significantly increased (p less-than 0.01). The NSCs did not significantly differ from each other in their ability to effect this rescue. (NASBG staining of neural cells from a wildtype mouse served as a positive control and were nearly 100% NASBG+, histogram not presented).
   (N) Complementation of gene product deficiency results in rescue of a
  pathologic phenotype in mutated neural cells, as illustrated by
  percentage of Tay-Sachs CNS cells with diminished GM2 accumulation. Among
 percentage of Tay-Sachs CNS cells with diminished GM2 accumulation. Among Tay-Sachs cells not exposed to NSCs (1st histogram), the percentage of GM2+ cells was large reflecting their pathologically high level of storage and consistent with a lack of enzyme as per (M). In contrast, the percentage of cross-corrected Tay-Sachs cells without detectable GM2 storage following exposure to murine (2nd and 3rd histograms, as in (M)) or human NSCs (4th histogram) was significantly lower than in the mutant (p less-than 0.01), approaching that in wildtype (+/+) mouse brain (5th histogram). Again, the NSCs did not significantly differ from each other in their ability to effect this rescue.
FIGS. 4A-4E: Developmentally-appropriate migration of human neural stem cells (NSCs) following engraftment into the subventricular germinal zone (SVZ) of newborn mice. (A,B) Donorderived human NSCs integrate and intermingle nondisruptively with endogenous progenitors within the host SVZ by 24 hours after transplantation. A representative donor-derived cell with a typical short process highlighted in (A), has interspersed with densely packed endogenous SVZ cells visualize by DAPI (blue) in the
  with densely packed endogenous SVZ cells, visualize by DAPI (blue) in the overlapping image in (B). (C) Two weeks following transplantation, many donor-derived cells (red) have migrated extensively within the
  subcortical white matter (arrow) and corpus callosum (c) from their site of implantation in the lateral ventricles (LV), as visualized in this coronal section. A representative migrating cell within the subcortical white matter (arrow), visualized at higher magnification in the boxed in corpus callosed to have a loading process.
  insert, is noted to have a leading process characteristic of migrating precursor cells. (D,E) As seen in this representative cresyl
  violet-counterstained parasagittal section, other donorderived cells
  migrated from their integration site in the anterior SVZ to enter the rostral migratory stream ("RMS") leading to the olfactory bulb ("OB")
  Representative BrdUimmunoperoxidase-positive (brown) donor-derived cells (arrow) within the RMS, are seen at low power in (D) and visualized at higher magnification in (E), intermixed with migrating host cells. Further characterization and visualization of these donor human
  NSC-derived cells in their final location in the OB are presented in FIG.
   5. Scale Bars: 100 mu m.
FIGS. 5A-5Q: Differentiation and disseminated foreign gene (
  beta-galactosidase) expression of human neural stem cell (NSC) clones in
  vivo following engraftment into the SVZ of developing, neonatal mice.

(A-C) Stably engrafted, beta-galactosidase (beta gal)-expressing, donor-derived cells from representative human NSC clone H1, detected with Xgal histochemistry (A,B) and with anti-beta gal ICC (C). The donor-derived cells pictured in the series of photomicrographs in (A) are within the periventricular and subcortical white matter regions (as per FIG. 4). (The top and bottom panels-low power on the left, corresponding high power on the right-are from representative semi-adjacent regions
  high power on the right-are from representative semi-adjacent regions
  within a single recipient, suggesting a significant distribution of cells; arrows indicate the lateral ventricles). Furthermore, as
  illustrated in (B,C) by representative high power photomicrographs through the olfactory bulb (OB) (located as in FIG. 4D), donor-derived
   cells from this clone have not only migrated extensively to this
   developmentally-appropriate site, but continue to express beta gal in
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normal fate of a subpopulation of SVZderived progenitors that have migrated to the OB at this developmental stage is to become neuronal. In (D-G), donorderived neurons in the mature OB, derived from BrdU-labeled NSCs (representative clone H6) implanted into the SVZ at birth, are identified by both their immunoreactivity to a humanspecific NF antibody (D) as well as their expression of the mature neuronal marker, NeuN (D) as well as their expression of the mature neuronal marker, NeuN (E-G); under confocal microscopy, a BrdU+ (hence, donor-derived) cell (arrow in (E), fluorescein) is NeuN+ (arrow in (F), Texas Red) appreciated best with a dual filter (arrow in (G)). Adjacent to this representative donorderived BrdU+/NeuN+ neuron (arrow), are 2 host OB neurons (BrdU/NeuN+ in (G)) which share a similar size, morphology, and location with the donor-derived cell (arrow in F). (H,I) High power view of a representative donor-derived (clone H6) oligodendrocyte (arrow), appropriately in the adult subcortical white matter (as per FIG. 4C) following neonatal intraventricular implantation, double-labeled with an antibody to the oligodendrocyte-specific protein CNPase (H) and BrdU (I). antibody to the oligodendrocyte-specific protein CNPase (H) and BrdU (I). Characteristic cytoplasmic processes extending from the some are noted (arrowhead in (H)). (The morphology of the CNPase+ cell has been somewhat damaged by the HCl pre-treatment required for BrdU double-labeling). (J) Mature donor-derived astrocytes (clone H6) in the adult subcortical white matter (arrow) (as per FIG. 4C) and striatum following neonatal intraventricular implantation, identified with a human-specific anti\*\*\*GFAP\*\*\* antibody. The inset better illustrates at higher magnification the characteristic mature astrocytic morphology of a representative human- \*\*\*GFAP\*\*\* + cell. (K-Q) Expression of vmyc is downregulated within 48 hours following engraftment. (K), (M), and (O) are DAPI-based nuclear stains of the adjacent panels (L), (N), and (P, Q), respectively. Representative human NSC clone H6 was generated (as was the well-characterized murine NSC clone C17.2) with the propagating gene vmyc. vmyc immunoreactivity in H6-derived cells (red) in the SVZ (arrows) at 24 hours following engraftment ((L) and at higher power in (N)), is persistently absent (P) in integrated H6-derived cells (visualized by BrdU labeling in (Q) (shown here 3 weeks following transplantation, but representative of any point 24 hours after engraftment). Scale Bars: (A), (K) and applies to (L): 100 mu m; (D), (E) and applies to (F,G), (H) and applies to (I), (J), (M) and applies to (N): 10 mu m; (O) and applies to (P,Q): 50 mu m representative human- \*\*\*GFAP\*\*\* + cell. (K-Q) Expression of vmyc is (P,Q): 50 mu mFIGS. 6A-6J: Neuronal replacement by human neural stem cells (NSCs) following transplantation into the cerebellum of the granule neuron-deficient meander tail (mea) mouse model of neurodegeneration.

(A-G) BrdU-intercalated, donor-derived cells (from representative clone (A-G) BrdU-intercalated, donor-derived cells (from representative clone H6) identified in the mature cerebellum by anti-BrdU immunoperoxidase cytochemistry (brown nuclei) following implantation into the neonatal measurement germinal layer (EGL). (The EGL, on the cerebellar surface, disappears as the internal granule layer (IGL) emerges to become the deepest cerebellar cortical layer at the end of organogenesis13) (A) Clone H6-derived cells are present in the IGL ("igl"; arrowheads) of all lobes of the mature cerebellum in this parasagittal section. (Granule neurons are diminished throughout the cerebellum with some prominence in the anterior lobe). (B) Higher magnification of the representative posterior cerebellar lobe indicated by arrowhead "b" in (A), demonstrating the large number of donor-derived cells present within the demonstrating the large number of donor-derived cells present within the recipient IGL. (C-G) Increasing magnifications of donor-derived cells (brown nuclei) within the IGL of a mea anterior cerebellar lobe. (Different animal from that in (A,B).) (G) Normarski optics bring out the similarity in size and morphology of the few residual host, BrdU-negative cerebellar granule neurons (arrowheads) and a BrdU+, donor-derived neuron (arrow), which is representative of those seen in all engrafted lobes of all animals.) (H,I) Confirmation of the neuronal differentiation of a subpopulation of the donor-derived, BrdU+ cells from (A-G) is illustrated by co-labeling with anti-BrdU (green in U) and the (A-G) is illustrated by co-labeling with anti-BrdU (green in H) and the mature neuronal marker NeuN (red in I) (indicated with corresponding arrows). (Some adjacent, donorderived cells are non-neuronal as indicated by their BrdU+ (arrowhead in (H)) but NeuN-phenotype (also illustrating the specificity of the immunostaining). (J) Cells within the IGL are confirmed to be human donor-derived cells by FISH with a human-specific probe (red) identifying human chromosomal centromeres. Scale Bars: (A), (B): 100 mu m; (F), (G), (J): 10 mu m!

ANSWER 9 OF 313 USPATFULL on STN 2004:253792 USPATFULL

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Persistent expression of candidate molecule in proliferating stem and progenitor cells for delivery of therapeutic products Rao, Mahendra S., Timonium, MD, UNITED STATES Capecchi, Mario R., Salt Lake City, UT, UNITED STATES

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 10 OF 313
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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        Selective antibody targeting of undifferentiated stem cells
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      ANSWER 12 OF 313 USPATFULL on STN
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AN
        Diagnosis and treatment of neuroectodermal tumors
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        Sontheimer, Harald W., Birmingham, AL, UNITED STATES
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        Lyons, Susan A., Monterallo, AL, UNITED STATES
        UAB Research Foundation (U.S. corporation)
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          Methods of treating neurological conditions with hematopoietic growth
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         Schaebitz, Wolf-Ruediger, Dossenheim, GERMANY, FEDERAL REPUBLIC OF Schneider, Armin, Heidelberg, GERMANY, FEDERAL REPUBLIC OF Krueger, Carola, Speyer, GERMANY, FEDERAL REPUBLIC OF Sommer, Clemens, Guenzburg, GERMANY, FEDERAL REPUBLIC OF Schwab, Stefan, Heidelberg, GERMANY, FEDERAL REPUBLIC OF Kollmar, Rainer, Heidelberg, GERMANY, FEDERAL REPUBLIC OF Maurer, Martin, Heidelberg, GERMANY, FEDERAL REPUBLIC OF Weber, Daniela, Mannheim, GERMANY, FEDERAL REPUBLIC OF Gassler, Nikolaus, Heidelberg, GERMANY, FEDERAL REPUBLIC OF AXARON BIOSCIENCE AG. Heidelberg, GERMANY, FEDERAL REPUBLIC OF
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           ICS: A61K038-19; A61K038-18
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          Enriched central nervous system stem cell and progenitor cell
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          populations, and methods for identifying, isolating and enriching for
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LN.CNT
          2296
           INCLM: 435/007.200
INCL
           INCLS: 435/368.000
NCLM: 435/007.200
NCL
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           NCLS:
                      435/368.000
IC
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           ICM: G01N033-53
           ICS: G01N033-567; C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       ANSWER 15 OF 313 USPATFULL on STN
L5
           2004:151408 USPATFULL
ΑN
           Molecules for diagnostics and therapeutics
TI
           Panzer, Scott R, Šunnyvale, CA, UNITED STATES
IN
           Lincoln, Stephen E, Potomac, MD, UNITED STATES Altus, Christina M, Campbell, CA, UNITED STATES
           Dufour, Gerard E, Castro Valley, CA, UNITED STATES Jackson, Jennifer L, Santa Cruz, CA, UNITED STATES
          Jones, Anissa L, San Jose, CA, UNITED STATES
Dam, Tam C, San Jose, CA, UNITED STATES
Liu, Tommy, Daly City, CA, UNITED STATES
Harris, Bernard, Sunnyvale, CA, UNITED STATES
Flores, Vincent Z, Union City, CA, UNITED STATES
Daffo, Abel, San Jose, CA, UNITED STATES
Marwaha, Rakesh Burnaby CANADA
           Marwaha, Rakesh, Burnaby, CANADA
Chen, Alice J, San Jose, CA, UNITED STATES
Chang, Simon C, Sunnyvale, CA, UNITED STATES
           Gerstin, Edward H, JR., San Jose, CA, UNITED STATES
Peralta, Careyna H, Santa Clara, CA, UNITED STATES
           David, Marie H, Daly City, CA, UNITED STATES
           Lewis, Samantha A, San Leandro, CA, UNITED STATES
                                                   20040617
ΡI
           US 2004115629
                                          A1
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WO 2002-US1009
Utility
                                  20020109
DT
       APPLICATION
FS
LN.CNT
       16703
INCL
       INCLM: 435/006.000
       INCLS: 435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.500
NCL
       NCLM:
               435/006.000
               435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.500
       NCLS:
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IC
       ICM: C12Q001-68
       ICS: C07H021-04; C07K014-47
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
                         USPATFULL on STN
     ANSWER 16 OF 313
L5
                     USPATFULL
       2004:150954
AN
TI
       Methods for treating disorders of neuronal deficiency with bone
       marrow-derived cells
       Blau, Helen M., Menlo Park, CA, UNITED STATES
Brazelton, Timothy, Cupertino, CA, UNITED STATES
Weimann, James M., Palo Alto, CA, UNITED STATES
The Board of Trustees of the Leland, Palo Alto, CA (U.S. corporation)
IN
PA
                                  20040617
PI
           2004115175
                            Α1
       US 2003-688747
                                  20031016 (10)
                            A1
ΑI
       Continuation-in-part of Ser. No. US 2001-993045, filed on 13 Nov 2001,
RLI
       PENDING
                              20001110 (60)
PRAI
       US 2000-247128P
DT
       Utility
       APPLICĀTION
FS
LN.CNT
       2455
INCL
        INCLM: 424/093.700
NCL
       NCLM:
               424/093.700
IC
        ICM: A61K045-00
L5
     ANSWER 17 OF 313
                         USPATFULL on STN
        2004:140277
                     USPATFULL
AN
       Multipotent adult stem cells, sources thereof, methods of obtaining
TI
        same, methods of differentiation thereof, methods of use thereof and
        cells derived thereof
                Leo T, Minneapolis, MN, UNITED STATES
IN
        Furcht
       Verfaillie, catherine M, St Paul, MN, UNITED STATES
       Reyes, Morayma, Minneapolis, MN, UNITED STATES
                                  20040603
        US 2004107453
                             A1
PI
                             Α1
                                   20040105 (10)
ΑI
       US 2004-467963
       WO 2002-US4652
                                  20020214
        Utility
DT
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FS
LN.CNT
       4100
        INCLM: 800/018.000
INCL
        INCLS: 424/093.700; 800/021.000; 435/353.000; 435/354.000; 435/366.000
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        NCLM:
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               424/093.700; 800/021.000; 435/353.000; 435/354.000; 435/366.000
        NCLS:
IC
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        ICM: A01K067-027
        ICS: C12N005-06; C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
                         USPATFULL on STN
     ANSWER 18 OF 313
L5
        2004:138675 USPATFULL
AN
        Promoting Recovery from Damage to the Central Nervous System
TI
        Finklestein, Seth P., 308A Hunnewell St, Needham, MA, UNITED STATES
IN
        Snyder, Evan Y., 22 Hillcroft Rd, Jamaica Plain, MA, UNITED STATES
        02130
       US 2004105847
US 2003-605456
                                   20040603
PI
                             Α1
                                   20030930 (10)
AΙ
                             Α1
        Continuation of Ser. No. US 2000-642277, filed on 18 Aug 2000, PENDING
RLI
        US 1999-149561P
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PRAI
        Utility
DT
        APPLICATION
FS
LN.CNT
       1943
INCL
        INCLM: 424/093.700
        INCLS: 514/012.000
        NCLM:
NCL
                424/093.700
        NCLS:
                514/012.000
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ICM: A61K045-00
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 19 OF 313 USPATFULL on STN
L5
         2004:94891 USPATFULL
AN
         Method for inducing differentiation of embryonic stem cells into
TI
         functioning cells
         Inoue, Kazutomo, Kyoto-shi, JAPAN
IN
         Kim, Dohoon, Kyoto-shi, JAPAN
Gu, Yanjun, Kyoto-shi, JAPAN
         Ishii, Michiyo, Kyoto-shi, JAPAN
                                        20040415
         US 2004072344
US 2003-626772
                                 A1
PI
                                        20030725 (10)
AΙ
                                 Α1
         Continuation-in-part of Ser. No. US 2002-54789, filed on 25 Jan 2002,
RLI
         PENDING
         Utility
DT
         APPLICATION
FS
LN.CNT
        1242
INCL
         INCLM: 435/366.000
         NCLM: 435/366.000
NCL
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IC
         ICM: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 20 OF 313
                             USPATFULL on STN
1.5
         2004:94213 USPATFULL
AN
         Method for therapeutically treating a clinically recognized form of
TI
         cardiopathology in a living mammal
Xiao, Yong-Fu, Wayland, MA, UNITED STATES
Morgan, James P., Newton Centre, MA, UNITED STATES
US 2004071665 Al 20040415
IN
PI
         US 2003-438574
                                         20030515 (10)
                                  A1
ΑI
         Continuation of Ser. No. WO 2002-US7555, filed on 14 Mar 2002, PENDING
RLI
         Continuation-in-part of Ser. No. US 2000-684679, filed on 7 Oct 2000,
         GRANTED, Pat. No. US 6607720 Continuation-in-part of Ser. No. US
         2000-655124, filed on 5 Sep 2000, GRANTED, Pat. No. US 6534052
DT
         Utility
         APPLICATION
FS
LN.CNT
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         INCLM: 424/093.700
INCL
NCL
         NCLM: 424/093.700
IC
         [7]
         ICM: A61K048-00
      ANSWER 21 OF 313 USPATE 2004:82751 USPATFULL
                             USPATFULL on STN
L_5
AN
TI
         Neurogenesis from hepatic stem cells
         Petersen, Bryon E., Gainesville, FL, UNITED STATES
Deng, Jie, Gainesville, FL, UNITED STATES
IN
PI
         US 2004063202
                                 A1
                                         20040401
         US 2003-651829
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                                         20030828 (10)
AΙ
                                  20020828 (60)
PRAI
         US 2002-406513P
DT
         Utility
         APPLICATION
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NCL
         NCLM:
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IC
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       ANSWER 22 OF 313 USPATFULL on STN
L5
         2004:63855 USPATFULL
AN
         Method for production of neuroblasts
Gage, Fred H., La Jolla, CA, UNITED STATES
Ray, Jasodhara, San Diego, CA, UNITED STATES
US 2004048373 A1 20040311
TI
IN
PΙ
         US 2003-622206
AΙ
                                         20030718 (10)
                                  Α1
         Continuation of Ser. No. US 2001-915229, filed on 24 Jul 2001, GRANTED, Pat. No. US 6599695 Continuation of Ser. No. US 1997-884427, filed on 27
RLI
         Jun 1997, GRANTED, Pat. No. US 6265175 Continuation of Ser. No. US
         1995-445075, filed on 19 May 1995, ABANDONED Division of Ser. No. US 1993-147843, filed on 3 Nov 1993, GRANTED, Pat. No. US 5766948 Continuation-in-part of Ser. No. US 1993-1543, filed on 6 Jan 1993,
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DT
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FS
             APPLICATION
LN.CNT 1641
INCL
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IC
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              ICM: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
         ANSWER 23 OF 313
                                             USPATFULL on STN
L5
                                    USPATFULL
              2004:63735
AN
TI
             Molecules for diagnostics and therapeutics
             Panzer, Scott R., Sunnyvale, CA, UNITED STATES
Spiro, Peter A., Palo Alto, CA, UNITED STATES
IN
             Banville, Steven C., Palo Alto, CA, UNITED STATES
              Shah, Purvi, San Jose, CA, UNITED STATES
             Chalup, Michael S., Sunnyvale, CA, UNITED STATES
Chang, Simon C, Mountain View, CA, UNITED STATES
Chen, Alice J., San Jose, CA, UNITED STATES
D'Sa, Steven A., East Palo, CA, UNITED STATES
Amshey, Stefan, San Francisco, CA, UNITED STATES
Dahl, Christopher E., Fremont, CA, UNITED STATES
Dam, Tam C., San Jose, CA, UNITED STATES
Daniels Susan E. Dalo Alto CA UNITED STATES
             Daniels, Susan E., Palo Alto, CA, UNITED STATES
Dufour, Gerard E., Castro Valley, CA, UNITED STATES
Flores, Vincent, Union City, CA, UNITED STATES
Fong, Willy T., San Francisco, CA, UNITED STATES
Greenawalt, Lila B., San Jose, CA, UNITED STATES
Jackson, Jennifer L., Mountain View, CA, UNITED STATES
Jones Anissa I. San Jose CA UNITED STATES
             Jones, Anissa L., San Jose, CA, UNITED STATES
Liu, Tommy F., Daly City, CA, UNITED STATES
Lincoln, Ann M. Roseberry, Redwood City, CA, UNITED STATES
Rosen, Bruce H., Menlo Park, CA, UNITED STATES
Russo, Frank D., Rossette Court Sunnyvale, CA, UNITED STATES
              Stockdreher, Theresa K., Sunnyvale, CA, UNITED STATES Daffo, Abel, San Jose, CA, UNITED STATES Wright, Rachel J., Mountain View, CA, UNITED STATES
              Yap, Pierre E., Lafayette, CA, UNITED STATES
Yu, Jimmy Y., Fremont, CA, UNITED STATES
Bradley, Diana L., Soquel, CA, UNITED STATES
Bratcher Charm B. Mountain View CA
             Bratcher, Shawn R., Mountain View, CA, UNITED STATES
Chen, Wensheng, Mountain View, CA, UNITED STATES
Cohen, Howard J., Palo Alto, CA, UNITED STATES
Hodgson, David M., Ann Arbor, MI, UNITED STATES
Lincoln, Stephen E., Redwood City, CA, UNITED STATES
Jackson, Stuart E., Mountain View, CA, UNITED STATES
US 2004048253
Al 20040311
PI
                                                   Α1
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AΙ
              US 2003-220120
              WO 2001-US6059
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DT
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FS
LN.CNT
             17872
              INCLM: 435/006.000
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              INCLS: 435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.500
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NCL
              NCLM:
              NCLS:
                            435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.500
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IC
               ICM: C12Q001-68
               ICS: C07H021-04; C07K014-47; A61K038-17
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
          ANSWER 24 OF 313 USPATFULL on STN
L5
              2004:44604 USPATFULL
Multipotent neural stemcells from peripheral tissues and uses thereof
AN
TI
              Toma, Jean, Toronto Ontario, CANADA
IN
              Akhavan, Mahnaz, Toronto Ontario, CANADA
Fernandes, Karl J. L., Toronto Ontario, CANADA
              Fortier, Mathieu, Orford, CANADA
              Miller, Freda, Toronto Ontario, CANADA
              Golster, Andrew, Saskatoon Sakatchewan, CANADA
PI
              US 2004033597
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                                                              20040219
AΙ
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              US 2003-181508
              WO 2001-CA47
KR 1999-34362
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PRAI
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DT
              Utility
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LN.CNT 1376
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                   435/371.000
          INCLS:
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NCL
         NCLM:
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         NCLS:
IC
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          ICM: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       ANSWER 25 OF 313
                                USPATFULL on STN
L5
                           USPATFULL
          2004:18785
AN
          Molecules for diagnostics and therapeutics
TI
         Hodgson, David M., Ann Arbor, MI, UNITED STATES
Lincoln, Stephen E., Potomac, MD, UNITED STATES
Russo, Frank D., Sunnyvale, CA, UNITED STATES
Albany, Peter A., Berkeley, CA, UNITED STATES
Banville, Steve C., Sunnyvale, CA, UNITED STATES
Bratcher, Shawm P., Mountain View, CA, UNITED STATES
IN
         Bratcher, Shawn R., Mountain View, CA, UNITED STATES
Dufour, Gerard E., Castro Valley, CA, UNITED STATES
Cohen, Howard J., Palo Alto, CA, UNITED STATES
Rosen, Bruce H., Menlo Park, CA, UNITED STATES
Chalup, Michael S., Livingston, TX, UNITED STATES
          Jackson, Jennifer L., Santa Cruz, CA, UNITED STATES
          Jones, Anissa L., San Jose, CA, UNITED STATES
Yu, Jimmy Y., Fremont, CA, UNITED STATES
          Greenawalt, Lila B., San Jose, CA, UNITED STATES Panzer, Scott R., Sunnyvale, CA, UNITED STATES
          Roseberry Lincoln, Ann M., Potomac, MD, UNITED STATES Wright, Rachel J., Merivale, NEW ZEALAND Daniels, Susan E., Mountain View, CA, UNITED STATES
          Incyte Corporation, Palo Alto, CA, UNITED STATES (U.S. corporation)
PA
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                                             20040122
          US 2004014087
PI
                                             20030228 (10)
ΑI
          US 2003-378029
                                     Α1
          Continuation-in-part of Ser. No. US 2001-980285, filed on 30 Nov 2001, PENDING A 371 of International Ser. No. WO 2000-US15404, filed on 31 May
RLI
          2000, PENDING
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          US 1999-147500P
PRAI
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                                                    (60)
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          US 1999-147824P
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          US 1999-147547P
          US 1999-147530P
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                                                    (60)
          US 1999-147536P
          US 1999-147520P
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          US 1999-137411P
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                                       19990602
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DT
          Utility
          APPLICATION
FS
          14819
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INCL
          INCLM: 435/006.000
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          INCLS:
                     530/388.260; 536/023.200; 800/008.000
NCL
                    435/006.000
          NCLM:
                    435/007.100; 435/069.100; 435/183.000; 435/320.100; 435/325.000;
          NCLS:
                     530/388.260; 536/023.200; 800/008.000
IC
           ICM: C12Q001-68
          ICS: G01\tilde{N}033-53; A01K067-00; C07H021-04; C12N009-00; C12P021-02;
          C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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2004:13073
                     USPATFULL
AN
        Oligodendrocytes derived from human embryonic stem cells for
TI
        remyelination and treatment of spinal cord injury
        Keirstead, Hans S., Irvine, CA, UNITED STATES
Nistor, Gabriel I., Placentia, CA, UNITED STATES
IN
        US 2004009593
                              A1
                                     20040115
ΡI
                                     20030404 (10)
ΑI
        US 2003-406817
                               Α1
        US 2002-395382P
                                20020711 (60)
PRAI
DT
        Utility
        APPLICÂTION
FS
LN.CNT
        1704
        INCLM: 435/368.000
INCL
                435/368.000
        NCLM:
NCL
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IC
        ICM: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 27 OF 313 USPATFULL on STN
L5
        2004:13072 USPATFULL
NA
        Genetically-modified neural progenitors and uses thereof
ΤI
        Sabate, Olivier, Paris, FRANCE
IN
        Horellou, Philippe, Paris, FRANCE
        Buc-Caron, Marie-Helene, Paris, FRANCE
        Mallet, Jacques, Paris, FRANCE
        Rhone-Poulenc Rorer S.A. (non-U.S. corporation)
PA
        US 2004009592
                               A1
                                     20040115
ΡI
                                                (10)
                                     20021127
ΑI
        US 2002-305386
                               A1
        Continuation of Ser. No. US 1997-810315, filed on 28 Feb 1997, ABANDONED
RLI
        US 1996-12635P
                                19960301 (60)
PRAI
        Utility
DT
        APPLICATION
FS
LN.CNT
        1050
        INCLM: 435/368.000
INCL
                435/368.000
NCL
        NCLM:
IC
        [7]
        ICM: C12N005-08
    INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 28 OF 313 USPATFULL on STN 2004:7427 USPATFULL
L5
ΝA
        Potential growth factors from the human tumour cell line ht 1080
TI
        Minger, Stephen L., London, UNITED KINGDOM
IN
        Adams, Gregor, London, UNITED KINGDOM
        Francis, Paul, London, UNITED KINGDOM
        Mcclure, Myra, London, UNITED KINGDOM
        US 2004005661
                                     20040108
PΙ
                               A1
        US 2003-344503
                                     20030708
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ΑI
        WO 2001-GB3523
                                     20010806
                                20000810
        GB 2000-19705
Utility____
PRAI
DT
        APPLICATION
FS
LN.CNT
        1664
         INCLM: 435/069.100
INCL
         INCLS: 435/226.000; 435/320.100; 435/366.000; 530/350.000; 536/023.200
NCL
                 435/069.100
        NCLM:
                 435/226.000; 435/320.100; 435/366.000; 530/350.000; 536/023.200
        NCLS:
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IC
         ICM: C12N009-64
         ICS: C07H021-04; C12N005-08; C07K014-47; C12P021-02
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 29 OF 313 USPATFULL on STN
L5
         2004:223722 USPATFULL
AN
        Cell expansion system for use in neural transplantation Studer, Lorenz, New York, NY, United States McKay, Ron D., Bethesda, MD, United States The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. corporation) US 6787356 B1 20040907
TI
IN
PA
PΙ
                          20000203
         WO 2000005343
                                      20010316 (9)
         US 2001-744384
AΙ
         WO 1999-US16825
                                      19990723
                                 19980724 (60)
PRAI
         US 1998-93991P
DT
         Utility
FS
         GRANTED
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INCLM: 435/377.000
INCL
         INCLS: 435/325.000; 435/384.000; 424/093.210; 514/044.000
                 435/377.000
NCL
        NCLM:
                 435/325.000; 435/384.000; 424/093.210; 514/044.000
        NCLS:
IC
         [7]
         ICM: C12N005-02
         ICS: A61K048-00
         435/377; 435/324; 435/384; 435/325; 924/93.21; 514/44
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 30 OF 313 USPATFULL on STN
L5
         2004:223721 USPATFULL
AN
        Multipotent neural stem cells from peripheral tissues and uses thereof
TI
        Miller, Freda D., Montreal, CANADA
IN
        Gloster, Andrew, Saskatoon,
                                           CANADA
         Toma, Jean, Montreal, CANADA
         McGill University, Montreal, CANADA (non-U.S. corporation)
PA
                                      20040907
         US 6787355
                                В1
PI
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ΑI
        US 2000-670049
        Continuation-in-part of Ser. No. US 2000-490422, filed on 24 Jan 2000 Continuation-in-part of Ser. No. US 1997-920272, filed on 22 Aug 1997
RLI
                                 19960827
                                            (60)
        US 1996-24456P
US 1996-24590P
PRAI
                                 19960826
                                             (60)
DT
         Utility
FS
         GRANTED
LN.CNT
        1239
         INCLM: 435/377.000
INCL
        INCLS: 435/378.000; 435/375.000; 435/383.000; 435/325.000

NCLM: 435/377.000

NCLS: 435/378.000; 435/375.000; 435/383.000; 435/325.000
NCL
         [7]
IC
         ICM: C12N005-00
         ICS: C12N005-02; C12N015-00
         435/377; 435/387; 435/375; 435/383; 435/325; 435/7.21
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 31 OF 313
                           USPATFULL on STN
L5
         2004:223720 USPATFULL
AN
         Lineage-restricted neuronal precursors and methods of isolation
TI
        Rao, Mahendra S., Salt Lake City, UT, United States
Mayer-Proschel, Margot, Sandy, UT, United States
Kalyani, Anjali J., Salt Lake City, UT, United States
University of Utah Research Foundation, Salt Lake City, UT, United
IN
PA
         States (U.S. corporation)
         US 6787353
                                       20040907
PI
                                B1
                                       19980702 (9)
         US 1998-109858
AΙ
         Continuation-in-part of Ser. No. US 1997-909435, filed on 4 Jul 1997
RLI
DT
         Utility
         GRANTEĎ
FS
LN.CNT 2022
INCL
         INCLM: 435/368.000
         INCLS: 435/377.000
NCL
         NCLM:
                 435/368.000
                 435/377.000
         NCLS:
IC
         [7]
         ICM: C12N005-08
         435/352; 435/366; 435/368; 435/377; 435/345; 435/350; 435/351; 435/455;
EXF
         424/932
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 32 OF 313 USPATFULL on STN
L5
         2004:186665 USPATFULL
AN
         Method of isolating adult mammalian CNS-derived progenitor stem cells
TI
         using density gradient centrifugation
         Gage, Fred H., La Jolla, CA, United States
Palmer, Theo, San Carlos, CA, United States
Safar, Francis G., Irvine, CA, United States
IN
         Takahashi, Jun, Kyoto, JAPAN
Takahashi, Masayo, Kyoto, JAPAN
         The Salk Institute for Biological Studies, La Jolla, CA, United States
PA
         (U.S. corporation)
                                       20040727
PI
         US 6767738
                                 B1.
                            20000817
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        GRANTED
FS
LN.CNT
        2082
        INCLM: 435/325.000
INCL
        INCLS: 435/366.000; 435/368.000; 435/378.000
                 435/325.000
NCL
                 435/366.000; 435/368.000; 435/378.000
        NCLS:
IC
         [7]
         ICM: C12N005-02
        ICS: C12N005-08
435/325; 435/352; 435/354; 435/363; 435/366; 435/368; 435/378; 435/7.21;
435/29; 435/240.1; 435/240.2; 435/240.21; 435/240.23; 435/384; 435/405;
435/406; 435/395; 435/402; 536/23.1
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L5
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AN
        Methods, compositions and kits for promoting recovery from damage to the
TI
         central nervous system
         Finkelstein, Seth P., Needham, MA, United States
Snyder, Evan Y., Jamaica Plain, MA, United States
IN
         The General Hospital Corporation, Boston, MA, United States (U.S.
PA
         corporation)
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         corporation)
                                       20040615
PΙ
                                 В1
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                                       20000818 (9)
AΙ
         US 1999-149561P
                                  19990818 (60)
PRAI
DT
         Utility
FS
         GRANTED
LN.CNT
        2033
         INCLM: 424/093.700
INCL
         INCLS: 424/093.100; 514/012.000
                  424/093.700
NCL
                 424/093.100; 514/012.000
         NCLS:
IC
         [7]
         ICM: A61K035-14
         ICS: A61K038-08
EXF 424/93.7; 424/198.1; 514/12
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AN
         Isolation of lineage-restricted neuronal precursors
ΤI
         Rao, Mahendra S., Salt Lake City, UT, United States Mayer-Proschel, Margot, Sandy, UT, United States
IN
         University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)
PA
         US 6734015
                                 В1
                                       20040511
PΤ
AΙ
         US 1997-909435
                                       19970704 (8)
         Utility
DT
         GRANTED
FS
LN.CNT
        967
         INCLM: 435/368.000
INCLS: 435/325.000
NCLM: 435/368.000
NCLS: 435/325.000
INCL
NCL
         [7]
IC
         ICM: C12N005-00
         ICS: C12N005-06; C12N005-08
         435/350; 435/351; 435/352; 435/325; 435/368; 435/363; 435/353; 435/354; 435/366; 435/377; 435/378; 435/383; 435/384; 435/387
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 35 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation.
L5
                                                                       DUPLICATE 9
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AN
       2004:243501 BIOSIS
DN
       PREV200400246287
      Mitotic and neurogenic effects of dehydroepiandrosterone (DHEA) on human neural stem cell cultures derived from the fetal cortex.
TI
       Suzuki, Masatoshi; Wright, Lynda S.; Marwah, Padma; Lardy, Henry A.;
ΑU
       Svendsen, Clive N. [Reprint Author]
       1500 Highland Avenue, T611 Waisman Center, Madison, WI, 53705, USA
CS
       svendsen@waisman.wisc.edu
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(March 2 2004) Vol. 101, No. 9, pp. 3202-3207. print. America, ISSN: 0027-8424 (ISSN print). DTArticle LA English Entered STN: 6 May 2004 ED Last Updated on STN: 6 May 2004 L5 ANSWER 36 OF 313 MEDLINE on STN AN IN-PROCESS 2004515453 PubMed ID: 15485786 DN Isolation, culture and identification of rat hippocampal neural stem TI cells. Guo Hong-Bo; Zou Fei Department of High-temperature Medicine, Southern Medical University, AII CS Guangzhou 510515, China. Di yi jun yi da xue xue bao = Academic journal of the First Medical SO College of PLA, (2004 Oct) 24 (10) 1143-6. Journal code: 9426110. ISSN: 1000-2588. CYChina Journal; Article; (JOURNAL ARTICLE) DT Chinese LА IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals FS Entered STN: 20041017 EDLast Updated on STN: 20041017 L5ANSWER 37 OF 313 MEDLINE on STN 2004449582 IN-PROCESS ANPubMed ID: 15357439 DN Purification, induced differentiation and identification of rat embryonic TI neural stem cells. Liu Fuyun; Liu Wenying; Shi Hong; Hu Tingze; Liu Lijun Department of Pediatric Surgery, West China Hospital of Sichuan ΑU CS University, Chengdu 610041, China. Sheng wu yi xue gong cheng xue za zhi = Journal of biomedical engineering SO = Shengwu yixue gongchengxue zazhi, (2004 Aug) 21 (4) 591-6. Journal code: 9426398. ISSN: 1001-5515. CY China Journal; Article; (JOURNAL ARTICLE) DTLА Chinese IN-PROCESS; NONINDEXED; Priority Journals FS Entered STN: 20040911 ED Last Updated on STN: 20040911 L5 ANSWER 38 OF 313 EMBAL COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 10 2004374969 EMBASE Alert (EMBAL) ANVigorous neuronal differentiation of amplified and grafted basic TIfibroblast growth factor-responsive neurospheres derived from neuroepithelial stem cells. ΑU Yamada M.; Uchida K.; Hayashi T.; Mine Y.; Kawase T. Dr. K. Uchida, Department of Neurosurgery, School of Medicine, Keio University, Shinanomachi 35, Shinjuku-ku, Tokyo 160-8582, Japan. CS koichi@sc.itc.keio.ac.jp Cell Transplantation, (2004) 13/4 (421-428). Refs: 24. SO ISSN: 0963-6897 CODEN: CTRÃE CY United States DT Conference Article English LA SL English EMBAL COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. L5ANSWER 39 OF 313 DUPLICATE 11 2004417669 EMBASE Alert (EMBAL) ΑN Comparative study of inducing differentiation of adult rat bone marrow TIstromal cells into neurons by various neurotrophic factors and antioxidant. Ye M.; Chen S.-D.; Lu G.-Q.; Liang L.; Liu W.-G. M. Ye, Department of Neurology, Ruijin Hospital, Shanghai Second Medical AII CS University, Shanghai 200025, China SO Chinese Journal of Neuroscience, (2004) 20/4 (275-280). Refs: 7. CODEN: ZSKZF ISSN: 1008-0872 CY China Article DT LAChinese

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  Lab. of Mol. Neuropharmacol., Grad. Sch. Pharm. Sci., Osaka Univ., Suita, ΑU
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  Gorio A.; Torrente Y.; Madaschi L.; Di Stefano A.B.; Pisati F.; Marchesi C.; Belicchi M.; Di Giulio A.M.; Bresolin N.
  A. Gorio, Dept. of Med., Surgery and Dentistry, Faculty of Medicine,
  University of Milan, Via A di Rudini 8, Milano 20142, Italy. CS E-mail: alfredo.gorio@unimi.it
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  Department of Anatomical Sciences and Neurobiology, School of Medicine, University of Louisville, 500 South Preston Street, HSC-A916, Louisville, CS KY, 40292, USA
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- Department of Anatomy, School of Medicine, Ajou University, Suwon, CS 442-749, South Korea hysuh@ajou.ac.kr
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- CS Department of Anatomy and Neurobiology, Medical College of Virginia, Virginia Commonwealth University, PO Box 980709, Richmond, VA 23298-0709, USA.
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- Journal; Article; (JOURNAL ARTICLE) DT
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- Entered STN: 20040406 Last Updated on STN: 20040720 Entered Medline: 20040719
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- PBChinese Journal of Traumatology (English Edition)
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- ISBN: 91-628-5666-9.
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- FS DAI
- LAEnglish
- Entered STN: 20040107 ED
  - Last Updated on STN: 20040107

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L5
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       2003-23517
                    BIOTECHDS
AN
      Making a cDNA library, useful for treating neurodegenerative diseases, e.g. Parkinson's or Alzheimer's disease, comprises proliferating
TI
       multipotent neural stem cells on an adherent substrate or in a suspension
          cell culture differentiation and proliferation and DNA library
      production for use in gene therapy and tissue engineering WEISS S; REYNOLDS B; HAMMANG J P; BAETGE E E WEISS S; REYNOLDS B; HAMMANG J P; BAETGE E E
ΑU
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PRAI
       Patent
DT
LΑ
       English
       WPĪ: 2003-626207 [59]
OS
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L5
       DUPLICATE 17
       2003-22551
                    BIOTECHDS
AN
       Proliferating a culture of undifferentiated neural cells containing
TI
       multipotent neural stem cells for treating neural disorders by culturing
       the cells in a culture medium containing a proliferation-inducing growth
       factor;
          stem cell proliferation and differentiation for use in tissue
          engineering and gene therapy
       WEISS S; REYNOLDS B; HAMMANG J P; BAETGE E E WEISS S; REYNOLDS B; HAMMANG J P; BAETGE E E US 2003095956 22 May 2003 US 2002-199918 19 Jul 2002
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AI
       US 2002-199918 19 Jul 2002; US 1991-726812 8 Jul 1991
PRAI
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       Patent
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LA
       WPĪ: 2003-606402 [57]
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DN
      138:217803
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ΤI
IN
      Brown, Patrick O.; Soen, Yoav; Keen, Erica
PA
SO
      U.S. Pat. Appl. Publ., 29 pp.
      CODEN: USXXĈŌ
DT
      Patent
LA
      English
FAN.CNT 1
                                                   APPLICATION NO.
                                                                              DATE
      PATENT NO.
                                     DATE
                             KIND
                                                                              20020702
PΙ
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                              Α1
                                     20030306
                                                   US 2002-190425
                                                                              20020702
                                                   WO 2002-US21162
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      WO 2003058193
                              A2
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                              Α3
      WO 2003058193
               AU, CA, JP
          W:
          RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
                                                   EP 2002-804103
                                                                              20020702
                              Α2
                                     20040428
      EP 1412535
                             DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               AT, BE, CH,
          R:
                             TR, BG, CZ, EE,
               IE, FI, CY,
                                                SK
                                     20010702
PRAI US 2001-303109P
                              P
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                              W
                                     20020702
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                           IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 19
L5
       10481730 IFIPAT; IFIUDB; IFICDB
AN
       CANCER MODELS
TI
       Bachoo Robert M; Depinho Ronald A
IN
       Unassigned Or Assigned To Individual (68000)
PA
                              20031204
PI
       US 2003226159
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                                        (Provisional)
FI
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                              20031204
       Utility; Patent Application - First Publication
DT
FS
       CHEMICAL
       APPLICATION
CLMN
       29
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FIG. 1. Comparison of Ink4a/Arf+/+ and -/-neural stem cells (NSCs) and
    astrocytes. A. NSC morphology (upper panels) and ***nestin***
staining (inset upper panels) of neurospheres is similar for Ink4a/Arf+/+
and -/-cultures. Astrocyte morphology (lower panels) and ***GFAP***
staining (inset lower panels) is also similar between Ink4a/Arf+/+ and
-/-cultures. B. The total number of ***EGF*** responsive NSCs
isolated from Ink4a/Arf+/+ and -/-brains at E8.5 (n=4), E10.5 (n=9),
E13.5 (n=38), E17.5 (n=12), P1 (n=16), and adult (6 weeks, n=4). C. The
total number of neurospheres generated in defined media with ***EGF***
(20 ng/mL), without ***EGF***, and with PDGF (50 ng/mL). Data
represent the means +/-the standard error of the mean (SEM) of the number
      represent the means +/-the standard error of the mean (SEM) of the number
     of stem cells residing in the striatal germinal zone at E13.5 (n=32-38 embryos per genotype). D. Differentiation of Ink4a/Arf-/-NSCs (
***nestin*** positive) into astrocytes ( ***GFAP*** positive, lower left) in response to serum and neurons (TUJ1, lower right) in response to
                                                                                                                                                                                                                                                                                                                                        positive, lower
      BDNF.
 FIG. 2. p16INK4a and p19ARF cooperate to regulate the growth of astrocytes but not NSCs. Growth during serial passage by Ink4a/ Arf genotype for A.
NSCs and B. astrocytes. C. Number of persistently growing astrocytes lines (i.e., "non-senesced"; Sharpless et al., Nature, 413:86-91 (2001)) by passage and p16INK4a and p19ARF status. D. Western blot analysis of p16INK4a and p19ARF in NSCs and astrocytes by Ink4a/Arf genotype. +Control=p16INK4a and p19ARF overexpressing tumor cell line.

FIG. 3. Ink4a/Arf-/-astrocytes dedifferentiate to ***nestin*** +, A2B5+ progenitor cells in vitro. Ink4a/Arf+/+ (A) and -/-(B) cells were removed from serum and grown in ***EGF*** on day 0. Ink4a/Arf-/-cells rapidly change morphology and resulting bipolar cells and neurospheres are ***nestin*** + and A2B5+ (double labeling inset, far right panel of B), whereas Ink4a/Arf+/+ cells do not dedifferentiate and remain ***GFAP*** + (inset, far right panel of A). Western blot analysis of
       NSCs and B. astrocytes. C. Number of persistently growing astrocytes
      ***GFAP*** + (inset, far right panel of A). Western blot analysis of cultured astrocytes of indicated genotypes after treatment with 
***EGF*** . C) Equivalent MAPK, AKT and D) EGFR phosphorylation is seen in Ink4a/Arf-/- and +/+ cells after ***EGF*** exposure.

***nestin*** and ***GFAP*** expression in the brains of adult
       ***nestin*** and ***GFAP*** expression in the brains of adult Ink4a/Arf+/+ (A) and -/-(B) mice after intraventricular ***EGF*** infusion. Images (low and high power H&E, ***nestin*** and Olig2 staining) of E) Ink4a/Arf+/+ and F)-/-mice after intraventricular for 7 days of ***EGF***
                                                              ***EGF*** . Arrows (3E) indicate a welldifferentiated
       ependymal layer of single cell that is replaced by an expanded population
 of poorly differentiated progenitor cells (bracket, 3F).

FIG. 4. Expression of EGFR* in Ink4a/Arf-/-NSCs and astrocytes induces high-grade gliomas. Tumors derived from orthotopically transplanted Ink4a/Arf-/-EGFR* (A) NSCs and (B) astrocytes are gadolinium enhancing on MRI, grow as poorly differentiated highgrade tumors (40 x H&E), and express ***GFAP***, ***nestin***, and olig2.
 express ***GFAP*** , ***nestin*** , and olig2.

FIG. 5. A. p53-/-, p16INK4a-/- and p19ARF-/-astrocytes do not differentiate in response to ***EGF*** . Cultures were grown in serumfree media supplemented with ***EGF*** (20 ng/mL) for 10 days. In contrast to Ink4a/Arf-/-astrocytes, p53-/-, p16INK4a-/-, and p19ARF-/-astrocytes did not change morphology in response to ***EGF** and remained ***GFAP*** + and ***nestin*** -(insets represent double labeling with ***GFAP*** (red) and ***nestin*** (green) (n=4 independently derived cell lines for an independent derived derived derived derived derived derived derive
        double labeling with ***GFAP*** (red) and ***nestin*** (n=4 independently derived cell lines for each genotype). B. Ink4a/Arf-/astrocytes expressing the wild-type EGFR do not
                                                                                                                                                                                                                                                                                                                                     ***EGF***
        dedifferentiate in serum-free media containing without
       Ink4a/Arf-/astrocytes expressing EGFR* dedifferentiate in serum-free media lacking ***EGF*** . D. Ink4a/Arf+/+ astrocytes expressing EGFR* do not dedifferentiate. E. EGFR* expression in NSCs can substitute for ligand. Ink4a/Arf-/-EGFR* NSC cultures were grown in serum free media without ***EGF*** . Ink4a/Arf-/-cultures transduced with the wild-type EGFR do not proliferate under these conditions, but rather undergo apoptosis (not shown). F. Subcutaneous tumors derived from Ink4a/Arf-/-astrocytes transduced with EGFR*. High grade, undifferentiated tumors were ***GFAP*** + ***nestin*** + and
                                                                                                                                                                                  ***GFAP***
                                                                                                                                                                                                                                                                                  ***nestin***
        undifferentiated tumors were
        Olig2+, similar to intracranially generated tumors. Similar histology and immunoreactivity to ***GFAP*** , ***nestin*** , and Olig2 were
        immunoreactivity to ***GFAP***, ***nestin***, and Olig2 were found in subcutaneous tumors derived from Ink4a/Arf-/-NSCs transduced with ECED* (not show) Contact the ECED* (not show) Contact 
        with EGFR* (not shown). G. Spindle-cell and epithelioid-cell morphology
         was seen in 1 tumor each derived from. All tumors demonstrated strong
        hEGFR* staining and were Sox10 positive as shown here for 1 tumor derived from Ink4a/Arf/-EGFR* astrocytes.
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ANSWER 52 OF 313 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 20 10463023 IFIPAT; IFIUDB; IFICDB ISOLATION AND TRANSPLANTATION OF RETINAL STEM CELLS

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Unassigned Or Assigned To Individual (68000)
PA
         US 2003207450
                                         20031106
PΙ
                                  A1
         US 2002-203105
                                         20020806
AΙ
         WO 2001-US4419
                                         20010212
                                                         PCT 371 date
                                         20020806
                                                        PCT 102(e) date
                                         20020806
         US 2003207450
                                         20031106
FI
         Utility; Patent Application - First Publication
DT
         CHEMICAL
FS
         APPLICATION
CLMN
       19 Figure(s).
FIG. 1 depicts phase-contrast views (left, A) and greenfluorescent protein (GFP) illumination views (right, B) of GFPexpressing, neuroretina-derived
GΙ
         retinal stem cell spheres at 3 days (top panel) and 6 days (bottom panel)
         after dissociation into single cell suspension.
       FIGS. 2A and 2B are photomicrographs of NRSCs in vitro, labeled with antibodies against retinal stem cell markers: Ki-67, expressed by mitotic cells (left, FIG. 2A) and ***nestin***, an intermediate filament protein in neurons cells and immature neurons (right, FIG. 2B).
        FIGS. 3A and 3B are photomicrographs of neuroretina-derived stem cells
         after their in vitro exposure to serum, labeled with an antibody against ***glial*** ***fibrillary*** ***acidic*** ***protein*** ,
                                     tro exposure co :-

***fibrillary***

'ar 'anti- ***GFAP***
             ***glial***
                                                                             , left, FIG. 3A) and an
         marker for astrocytes (anti-
         antibody against neurofilament of 200 kD, a marker for mature neurons
          (antiNF200; right, FIG. 3B).
        FIGS. 4A-4D are green fluorescent protein(GFP)-illuminated photomicrographs of four examples of mouse retinal explant recipient tissue (obtained postnatally on day 1), co-cultured with mouse retinal stem cell spheres for 7 days in vitro.
        FIGS. 5A and 5B are two exemplary in situ photomicrographs of "green", neuroretina-derived retinal stem cells (derived from GFP-expressing
         transgenic mice), 2 weeks after being grafted in a host adult rd-2 mouse
         eye, labeled with a red-labeled antibody specific for the
        photoreceptor-specific marker, rhodopsin.

FIGS. 6A-F are photomicrographs of "green" NRSCs grafted into various retinal sites, 2 weeks post-graft. FIGS. 6A-6C and FIGS. 6D-6F, respectively, show views of the same retinal site, under different illumination: GFP illumination (FIGS. 6A and 6D), red-labeled
         anti-rhodopsin antibodies (FIGS. 6B and 6E); and ordinary photomicrograph
          (FIGS. 6F).
        FIG. 7 is a confocal photomicrograph of "green" NRSCs grafted into an
          extra-ocular site, 2 weeks post-graft, labelled with red-labeled,
          anti-recoverin antibodies.
        FIG. 8 is a confocal photomicrograph of "green" NRSCs grafted into a
        retinal site, 2 weeks post-graft, labelled with antirecoverin antibodies. FIGS. 9A and 9B are photomicrographs showing GFP (green, FIG. 9A) and rhodopsin (red, FIG. 9B) expression in RD-2 mouse vitreous, 2 weeks
          after grafting.
        FIGS. 10A-10C are photomicrographs of the same graft site: retinal stem
         cells grafted to the subretinal space of adult retina "green" NRSC from transgenic GFP-expressing mice, grafted to the subretinal space of adult retina in lesioned B6 mouse subretinal space, 2 weeks after grafting. FIG. 10A shows GFP expression (green illumination); FIG. 10B shows recoverin expression (staining of cells with red-labeled anti-recoverin antibodies); and FIG. 10C shows an overlay or merged view of FIGS. 11A
          and 11B.
        FIGS. 11A-11C are confocal micrographs of the same graft site: "green"
          NRSC from transgenic GFP-expressing mice, grafted to the subretinal space
          of adult retina in lesioned B6 mouse subretinal space, 2 weeks after
          grafting. FIG. 11A shows GFP expression (green illumination); FIG. 11B shows recoverin expression (staining of cells with red-labeled anti-recoverin antibodies); and FIG. 11C shows an overlay or merged view
        of FIGS. 11A and 11B.
FIGS. 12A-12C show confocal micrographs of the same graft site: "green"
NRSC grafted into lesioned B6 mouse subretinal space, 4 weeks after
          grafting. FIG. 12A shows recoverin expression (staining of cells with
          red-labeled anti-recoverin antibodies); FIG. 12B shows GFP expression
          (green illumination); and FIG. 12C is an overlay or merged view of FIGS.
         FIG. 13 a low-power photomicrograph of cultured, human neuroretina-derived
          stem cells (hNRSCs), showing bipolar, multipolar, and round cells, with
          neuritic processes.
        FIG. 14 is a photomicrograph of hNRSCs undergoing cell division
        FIG. 15 is a low-power photomicrograph of cultured hNRSCs, showing
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FIG. 17 is a phase photomicrograph showing the mitotic profile of hNRSCs.
       FIG. 18 is a bright-field photomicrograph of hNRSCs, showing that they are
         not pigmented.
        FIGS. 19A-19C are sequentially timed photomicrographs of the same cultured hNRSC specimen, showing a retinal stem or progenitor cell undergoing cell division. FIG. 19A shows the stem/progenitor cell before mitosis; FIG. 19B shows it during mitosis; and FIG. 19C shows it just after mitosis (with 2 daughter nuclei). FIG. 19C also shows a classic profile of an
         early, neural stem/progenitor cell.
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       ANSWER 53 OF 313
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        CELL PRODUCTION; CULTURING AND DIFFERENTIATING EARLY PRIMITIVE ECTODERM-LIKE (EPL) TISSUES WITH SUBSEQUENT RECOVERY OF PLURIPOTENT NEURECTODERMAL CELLS; GENE THERAPY FOR NERVOUS SYSTEM DISORDERS
         Rathjen Joy (AU); Rathjen Peter David (AU)
         Unassigned Or Assigned To Individual (68000)
                                        20030717
         US 2003134413
                                 A1
         US 2002-181359
                                        20021203
         WO 2001-AU30
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US 2003134413
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         Utility; Patent Application - First Publication .
         CHEMICÂL
         APPLICATION
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         70
          15 Figure(s).
       FIG. 1
       FIG.
       FIG.
               3
       FIG. 4
       FIG. 5
       FIG. 6
       FIG. 7
       FIG. 8
       FIG. 9
FIG. 10
FIG. 11
FIG. 12
       FIG. 13
       FIG. 14
       FIG. 15
       ANSWER 54 OF 313
                                   IFIPAT
                                               COPYRIGHT 2004 IFI on STN DUPLICATE 22
         10337746 IFIPAT; IFIUDB; IFICDB
DIFFERENTIATION OF WHOLE BONE MARROW; CULTURING STEM CELL WITH FIBROBLAST
GROWTH FACTOR AND EPIDERMAL GROWTH FACTOR
         Ehtesham Moneeb; Kabos Peter; Yu John S
         Unassigned Or Assigned To Individual (68000)
                                 A1
                                        20030501
         US 2003082160
         US 2002-253759
                                        20020924
                                        20011025 (Provisional)
PRAI
         US 2001-334957P
                                        20030501
         US 2003082160
         Utility; Patent Application - First Publication
         CHEMICĀL
         APPLICATION
CLMN
           12 Figure(s).
        FIG. 1 depicts neural progenitor cells obtained from human bone marrow in
         accordance with an embodiment of the present invention. FIG. 1A depicts
         cells from whole bone marrow that, when plated on poly-D-lysine, form a monolayer that gives rise to distinct cellular spheres after four days in
         culture. FIG. 1B depicts the spheres of FIG. 1A at higher magnification; cells may be easily collected, sub-cultured, and propagated separately in the presence of growth factors. FIG. 1C depicts that the spheres, once differentiated, attach and cells start migrating outward (arrows indicate migrating cells). FIG. 1D depicts that the formed opposed detach from the
         migrating cells). FIG. 1D depicts that the formed spheres detach from the
         bottom and afterwards remain free-floating.
        FIG. 2 is executed in color and depicts neural progenitor cells obtained
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FIG. 16 is a low-power photomicrograph of cultured hNRSCs, developing long

sequence to be non-pigmented.

neuritic processes.

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invention. FIGS. 2A and 2B indicate that neurospheres (i.e., spheres derived from neural cells) and bone marrow-derived spheres, respectively, were morphologically indistinguishable. FIGS. 2C and 2D indicate that the pattern of \*\*\*neurospheres and bear marrow derived spheres. respectively. Muclei of neurospheres and bone marrow derived spheres, respectively. Nuclei of cells appear blue owing to being counterstained with 4',6-diamidino-2phenylindole (DAPI). FIG. 3 is executed in color and depicts neural progenitor cells obtained from human bone marrow in accordance with an embodiment of the present invention. FIG. 3A indicates that the bone marrow-derived spheres expressed the ectodermal marker vimentin. As depicted in FIG. 3B, a weak staining for fibronectin was also observed in the neural progenitor cells. As depicted in FIG. 3C, bone marrow-derived spheres exhibit strong expression of CD90, and, as depicted in FIG. 3D, the majority of the cells in spheres exhibit nuclear expression of Neurogenin 1.

FIG. 4 is executed in color and depicts a differentiation of bone marrow derived cells into neurons and glia in accordance with an embodiment of the present invention. After plating on a substrate in media devoid of growth factors, the bone marrowderived spheres attached, migrated away from the primary site of attachment, and displayed multiple morphologies, as depicted in FIG. 4A. FIGS. 4B and 4C depict neural progenitor cells of the present invention expressing the glial cell marker
\*\*\*fibrillary\*\*\* \*\*\*acidic\*\*\* \*\*\*protein\*\*\* \*\*\*glial\*\*\* ( \*\*\*GFAP\*\*\* after eight and nine days of differentiation, respectively (cellular nuclei counterstained with DAPI). FIGS. 4D and 4E depict neural progenitor cells of the present invention expressing the neuronal marker Neuron Specific Enolase (NSE) after eight days of differentiation (cellular nuclei counterstained with DAPI). Control colling and all colling and counterstained with DAPI). (cellular nuclei counterstained with DAPI). Scattered cells also expressed the later neuronal marker MAP2, as depicted in FIG. 4F. After transplantation of the bone marrow derived spheres into the hippocampus of a syngeneic animal, cells expressing NeuN were found, as depicted in FIG. 4G. Some of these cells appeared to integrate into the hippocampal structure, as depicted in FIG. 4H. FIGS. 4I, 4J and 4K depict a similar differentiation of bone marrow derived cells, with alternate antibodies used for immunocytochemistry. FIG. 4I depicts the use of the oligodendrocyte marker CNPase (1:400 Sigma) at 40 x magnification, while FIGS. 4J and 4K depict the use of the neuronal marker NF200 (1:100 Chemicon) at 20 x and 40 x magnification, respectively. FIG. 5 is executed in color and depicts a gene transfer to neural progenitor cells using a beta-galactosidase genebearing replication-deficient adenoviral vector in accordance with an embodiment of the present invention. FIG. 6 is executed in color and depicts neural progenitor cells infected with green fluorescent protein (GFP) bearing double herpes simplex virus type I in accordance with an embodiment of the present invention.
FIG. 7 is executed in color and depicts neurospheres generated from primary fetal brain culture in accordance with an embodiment of the present invention. FIG. 7A depicts neural progenitor cells grown into spherical aggregates. FIG. 7B depicts \*\*\*nestin\*\*\* expression by spherical aggregates. FIG. 7B depicts \*\*\*nestin\*\*\* expression by these neurospheres (nuclei counterstained with DAPI). Neurons expressed beta-III tubulin, astrocytes expressed \*\*\*GFAP\*\*\* , and oligodendrocytes expressed CNPase (FIGS. 7C, 7D, and 7E, respectively). FIG. 7F depicts expression of beta-galactosidase by neural progenitor cells infected in vitro with AdLacZ. Magnification 400 x for FIGS. 7B, 7C, 7D, and 7E;  $100 \times for FIGS$ . 7A and 7F. FIG. 8 is executed in color and depicts an intra-arterial delivery of neural progenitor cells into an experimentally induced ischemic lesion in accordance with an embodiment of the present invention. Single cells are distributed widely throughout the brain tissue (FIG. 8A). Transplanted cells exhibit tropism for injured basal ganglia (FIG. 8B; at 400 x magnification). FIG. 9 is executed in color and depicts neural progenitor cells tracking tumor cells in vivo in accordance with an embodiment of the present invention. FIG. 9A depicts a thin outgrowth of tumor cells deep into adjacent normal brain. FIG. 9B depicts a direct extension of tumor mass into adjacent tissue. FIG. 9C depicts a migration of glioma cells away from the primary tumor bed along a white matter tract. FIG. 9D depicts a tumor microsatellite independent of a main tumor mass. FIG. 9E depicts a high power photomicrograph of the microsatellite depicted in FIG. further depicting beta-galactosidasepositive neural progenitor cells interspersed with tumor cells. FIG. 9F shows an inoculation of neural progenitor cells (left panel) and a tumor mass (right panel) into which neural progenitor cells migrated from the opposite hemisphere (inset box). Neural progenitor cells appear blue (expressing betagalactosidase), whereas tumor cells appear red (hypercellular areas stained intensively

microsatellites. Arrows indicate disseminating neural progenitor cells closely following migrating pockets of tumor.
FIG. 10 is executed in color and depicts intratumoral CD4+ and CD8+ T-cell infiltration in accordance with an embodiment of the present invention. FIG. 10A depicts a flow cytometry analysis demonstrating intratumoral T-cell infiltration in brain tissue treated with neural progenitor cells secreting IL12 (left panel) and 3T3-IL-12 (center panel), and a comparative lack of infiltration in tissue treated with neural progenitor cells secreting LacZ (right panel). CD4+ (left panel) and CD8+ (right panel) intratumoral infiltration is depicted in tissue treated with neural progenitor cells secreting 3T3-IL-12, LacZ, and IL-12 (FIGS. 10B, 10C, and 10D, respectively). Aggregates appeared along the tumor/normal tissue boundary in tissue treated with neural progenitor cells secreting IL-12 (FIG. 10D, arrows indicate aggregates). FIG. 10E depicts a comparison of Tcell infiltration in comparable outgrowths from a primary tumor bed for tissue treated with neural progenitor cells secreting IL-12 and 3Y3-IL-12 (FIGS. 10E, left and right panels, respectively). "T" designates tumor and "N" designates normal brain tissue. Magnification 100 x for FIGS. 10B, 10C, and 10D, and 200 x for FIG. 10E.
FIG. 11 is executed in color and depicts transplantation of neural progenitor cells expressing GFP into rat hippocampus in accordance with an embodiment of the present invention. FIG. 11A depicts a migration of transplanted cells (green). FIG. 11B depicts individual cells expressing NSE (red) and GFP together with NSE (yellow). Transplanted cells were stained for NSE and exhibit GFP (green), NSE (red), and the merged image of green fluorescent protein (GFP) and NSE (green and red) (FIGS. 11C, 11D, and 11E, respectively). Magnification 100 x for FIG. 11A; 630 x for FIG. 11B; and 200 x for FIGS. 11C, 11D, and 11E.
FIG. 12 is executed in color and depicts neural progenitor cells, stained for LacZ, seen in the tumor outgrowth migrating out from the main tumor mass at 10 x (FIG. 12A) and 40 x (FIG. 12B) magnification. The sections comparison of Tcell infiltration in comparable outgrowths from a primary mass at  $10 \times (FIG. 12A)$  and  $40 \times (FIG. 12B)$  magnification. The sections were counterstained with hematoxylin. IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 23 ANSWER 55 OF 313 IFIPAT; IFIUDB; IFICDB 10324405 METHOD OF IN VITRO DIFFERENTIATION OF TRANSPLANTATABLE NEURAL PRECURSOR CELLS FROM PRIMATE EMBRYONIC STEM CELLS; DIFFERENTIATION OF PRIMATE EMBRYONIC STEM CELLS INTO NERVOUS SYSTEM TISSUE; OBTAIN PRIMATE EMBRYONIC STEM CELL, PROPAGATE IN CULTURE CONTAINING FIBROBLAST GROWTH FACTOR, RECOVER CELLS Duncan Ian David; Thomson James A; Zhang Su-Chun Unassigned Or Assigned To Individual (68000) A1 20030410 US 2003068819 US 2001-970382 20011003 US 2003068819 20030410 Utility; Patent Application - First Publication CHEMICAL APPLICATION CLMN 3 Figure(s). FIGS. IA-I. Differentiation and isolation of neural precursors from ES cells. (FIG. 1A) An attached EB grown in the presence of FGF2 for 5 days shows flattened cells at the periphery and small elongated cells congregated in the center. (FIG. 1B) By 7 days, many rosette formations (arrows) appeared in the differentiating EB center. The up-right inset is the 1-mu m section of the rosette stained with tolundance blue, showing EB columnar cells arranged in a tubular structure. Bar=20 mu m. (FIGS. 1C-E) Cells in a cluster of rosettes (low left) and a small forming rosette (center) are positive for \*\*\*nestin\*\*\* (FIG. 1C) and Musashi-1 (FIG. (center) are positive for \*\*\*nestin\*\*\* (FIG. 1C) and Musashi-1 (FIG. 1D) whereas the surrounding flat cells are negative. (FIG. 1E) A combined image of FIG. 1C and FIG. 1D with all cell nuclei labeled with DAPI. (FIG. 1F) After treatment with dispase for 20 minutes, the rosette formations retracted whereas the surrounding flat cells remained attached. (FIGS. 1G-I) Isolated cells are positively stained for \*\*\*nestin\*\*\* in a filamentous pattern (FIG. 1G), Musashi-1 in cytoplas (FIG. 1H), and PSA-NCAM mainly on membrane (FIG. 1I). All nuclei are

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stained with DAPI. Bar=100 mu m. FIGS. 2A-G. Characterization of ES cell-derived neural precursors in vitro. (FIG. 2A) BrdU incorporation by dissociated ES cell-derived neural precursors is elevated in the presence of FGF2 (20 ng/ml) but not with \*\*\*EGF\*\*\* (20 ng/ml) or LIF (5 ng/ml). This is representative data from one of 3 replicate experiments. \* indicates difference between the experimental group and the control group (p less-than 0.01, n=4, student t-test). (FIG. 2B) Differentiation of a cluster of ES cell-derived neural precursors for 3 weeks shows neurite bundles with cells migrating along

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that the majority of cells are beta III-tubulin+ neurons (red) and that only a few cells are ***GFAP*** + astrocytes (green). (FIG. 2D) After 45 days of differentiation, many more ***GFAP*** + astrocytes (green)
   45 days of differentiation, many more
  appear along with NF200+ neurites (red, yellowish due to overlapping with green ***GFAP*** ). (FIGS. 2E-G) ES cell-derived neurons with various
morphologies express distinct neurotransmitters such as glutamate (FIG. 2E), GABA (FIG. 2F) and the enzyme tyrosine hydroxylase (FIG. 2G). O4+ oligodendrocytes (arrows) are observed after 2 weeks of differentiation in a glial differentiation medium. Bar=100 mu m.

FIGS. 3A-K. Incorporation and differentiation of ES cell-derived neural precursors in vivo. Grafted cells are detected by in situ hybridization with a probe to the human alu-repeat element (FIGS. 3A-E, G) or an antibody to a human-specific nuclear antigen (FIG. 3E) (FIG. 3A)
   antibody to a human-specific nuclear antigen (FIG. 3F). (FIG. 3A)
   Individual donor cells in the host cortex of an 8-week-old recipient
  (arrows). (FIG. 3B) Extensive incorporation of ES cell-derived neural precursors in the hippocampal formation. Cells hybridized with the human alu probe are labeled with red dots (pseudo-colored). (FIG. 3C) Incorporated human cells in the vicinity of the hippocampal pyramidal layer at P14. (FIG. 3D) ES cell-derived cells in the septum of a 4-week-old recipient mouse. (FIG. 3E) High power view of an individual donor cell in the hypothalamus. Note the seamless integration between adjacent unlabeled host cells. (FIG. 3F) Donor cells in the striatum of a 4-week-old host detected with an antibody to a human-specific nuclear
   4-week-old host, detected with an antibody to a human-specific nuclear
   antigen. (FIG. 3G) Extensive migration of transplanted cells from the
  aqueduct into the dorsal midbrain. (FIG. 3H) Human ES cellderived neuron
  in the cortex of a 2-week-old host, exhibiting a polar morphology and long processes. The cell is double labeled with antibodies to a human-specific nuclear marker (green) and beta III-tubulin (red). (FIG. 3I) Network of donor-derived axons in the fimbria of the hippocampus,
   identified with an antibody to human neurofilament. (FIG. 3J)
   Donor-derived multipolar neuron, double labeled with an antibody
   recognizing the a and b isoforms of MAP2. (FIG. 3K) ES cell-derived
   astrocyte in the cortex of a 4-week-old animal, double labeled with the
   human nuclear marker (green) and an antibody to
                                                                                                                        ***GFAP***
                                                                                                                                                        (red).
  Note that all the double labelings are confocal images and are confirmed by single optical cuts. Bars: FIG. 3A, FIG. 3B, FIG. 3G 200 mu m; FIG. 3C, FIG. 3D 100 mu m; FIG. 3E, FIG. 3F, FIGS. 3H-K 10 mu m.
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ΑN
       MULTIPOTENT STEM CELLS FROM PERIPHERAL TISSUES AND USES THEREOF; CELLULAR
TI
       COMPOSITION FOR USE IN REGENERATION MEDICINE
      Akhavan Mahnaz (CA); Fernandes Karl J L (CA); Fortier Mathieu (CA); Miller Freda (CA); Toma Jean (CA)
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       CHEMICAL
       APPLICATION
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        31 Figure(s).
      FIGS. 1A-1G are photographs showing that mouse skin-derived MSCs are
       nestinpositive and are capable of differentiating into neurons, glia, and
       smooth muscle cells.
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FIG. 2 is a series of photographs showing that neonate and adult mouse skin-derived MSCs express both \*\*\*nestin\*\*\* (middle row) and fibronectin protein (bottom row).

FIG. 3A is a series of photographs showing western blot analysis for \*\*\*nestin\*\*\*, neurofilament M (NF-M) and \*\*\*GFAP\*\*\* in cells differentiated from neonate and adult mouse skin-derived MSCs.

FIG. 3B is a series of photographs showing that human skinderived MSCs express \*\*\*nestin\*\*\*.

FIG. 3C is a series of photographs showing that a subset of morphologically complex cells expressed \*\*\*nestin\*\*\* and beta

tubulin, a profile typical of newly-born neurons. FIG. 3D is a series of photographs showing that GFP positive cells are also positive for neuron-specific enolase.

oligodendrocyte precursors, on undifferentiated mouse skinderived MSCs. FIG. 4B is a photograph showing the expression of the oligodendrocyte marker galactocerebroside (GaIC) on cells differentiated from mouse skin-derived MSCs.

FIG. 5 is a series of photographs showing that the fate of mouse skin-derived MSCs can be manipulated by controlling plating conditions. FIG. 6 is a series of photographs showing that neonate and adult mouse skin-derived MSCs can differentiate as adipocytes.

FIGS. 7A and 7B are photographs showing that \*\*\*nestin\*\*\*

fibronectin-positive MSCs can be derived from mouse dermis.

FIGS. 8A and 8B are photographs showing that individual MSCs are multipotent. Clones derived from single cells contained NF-Mpositive cells (arrowheads) and CNPase-positive cells (arrows). Arrowheads indicate cells that only express \*\*\*GFAP\*\*\*, while arrows ind cells expressing both \*\*\*GFAP\*\*\* and CNPase. , while arrows indicate

FIGS. 9A and 9B are photographs of western blot analysis of cells differentiated from mouse skin-derived MSCs (FIG. 9A) or of MSCs

themselves (FIG. 9B)

FIG. 10 is a series of photographs showing the effect of various pharmacological agents on mouse skin-derived MSCs.

FIGS. 11A-11E are photographs of immunoprocessed sections of rat brains

into which mouse skin-derived MSCs were transplanted.

'IG. 12 shows that \*\*\*nestin\*\*\* +, fibronectin+skin-derived MSCs isolated from adult human scalp differentiate into cells that express a FIG. 12 shows that variety of neural and non-neural markers, as measured by immunocytochemistry with antibodies to beta III-tubulin (A), CNPase (B), and smooth muscle actin (C), and \*\*\*GFAP\*\*\* (D).

FIG. 13 are photographs of skin-derived stem cells plated in 15% FBS in the process of skills are photographs.

the presence of skeletogenic supplements and cultured for two weeks. The cells are stained with Alcian Blue which reveals nodules of

chondrocyte-associated acidic proteoglycans.

FIG. 14 are photographs of skin-derived stem cells plated in 15% FBS in the presence of skeletogenic supplements and cultured for three weeks. The cells are stained with Alizarin Red which identified osteoblast-associated calcium accumulations.

FIG. 15 are photographs of skin-derived stem cells plated in 15% FBS in the presence of skeletogenic supplements, cultured for three weeks, and co-stained with both Alcian Blue and Alizarin Red. Co-staining reveals that the calcium deposits occur within a layer of chondrocytic proteoglycan accumulation.

FIG. 16 are photographs of skin-derived stem cells plated in 15% FBS in the presence of skeletogenic supplements and cultured for 4-5 weeks, and demonstrate the formation of optically dense deposits indicative of bone

FIG. 17 shows that co-culture of GFP labeled skin-derived stem cells with cardiac myocytes induces expression of fetal cardiac actin. The expression of fetal cardiac actin co-localizes with GFP indicating that the differentiated cell is derived from the skin-derived stem cell.

FIG. 18 shows that co-culture of GFP labeled skin-derived stem cells with C2C12 cells induces expression of desmin. The expression of desmin co-localizes with GFP, and the morphology of this desmin expressing cell is indicative of a skeletal muscle cell.

FIG. 19 shows RT-PCR analysis of skin-derived MSCs grown in spheres (S),

plated in proliferation media for three days (3d), or plated in proliferation media for three days followed by two days in 5% serum (3d+2). The skin-derived MSCs express \*\*\*nestin\*\*\* , GATA-4, and stin\*\*\* , GATA-4, and Myf6.
\*\*\*nestin\*\*\* ), embryoid (3d+2). The skin-derived MSCs express Positive controls (+ve) are: E10 brain (for

bodies (for GATA-4), and muscle (for Myf6).

FIG. 20 shows that skin-derived MSCs express endodermal markers under certain differentiation conditions. Skin-derived MSCs were cultured under standard proliferation conditions in the presence or absence of B-27 supplement. Differentiation was induced by plating cells in the presence of nicotinamide, and the resulting differentiated cells were analyzed by quantitative RT-PCR. The graph demonstrates that skin-derived MSCs differentiated in the presence of nicotinamide express several markers of endodermal differentiation including GATA-4, HNF3 alpha, Is11, AFP, HNF3 beta, Ngn3, Pdx-1, and Insulin. Although cells proliferated in either the presence or the absence of B27 supplement can be induced to express endodermal markers, cells proliferated in B27 appear to express such markers to a higher degree.

FIG. 21 shows that agents, including therapeutic proteins and small molecules, influence the proliferation, differentiation, and/or survival of skin-derived stem cells. Cells were dissociated and plated in the presence of either 5% FBS, 5% FBS+retinoic acid (RA), or 5% FBS+BMP7. Cells were analyzed immunocytochemically for expression of neurofilament

FIG. 22 shows that the skin-derived stem cells of the invention are a cell population distinct from mesenchymal stem cells. Mesenchymal stem cells and skin-derived stem cells were cultured under identical conditions, and immunocytochemical analysis was performed using antibodies\_to

\*\*\*nestin\*\*\*, fibronectin, vimentin, and cytokeratin. The top panels are photographs of mesenchymal stem cells, and the bottom panels are photographs of the skinderived stem cells. Note not only the differences in protein expression, but also the differences in morphology between the

two cell types.
FIG. 23 shows that skin-derived stem cells isolated from human foreskin proliferate as non-adherent clusters in culture. The top panels show that skin-derived stem cells specifically isolated from the dermal layer of human foreskin proliferate as non-adherent clusters. In contrast to human central nervous system derived stem cells, the survival and proliferation of human skin-derived stem cells is not dependent on LIF. The bottom panels show that skin-derived stem cells isolated from foreskin express \*\*\*nestin\*\*\* and fibronectin.

FIG. 24 shows that skin-derived stem cells isolated from human foreskin differentiate to form highly morphologically complex neurons as assayed by expression of bIII-tubulin and neurofilament-M (NF-M).

FIG. 25 shows that skin-derived stem cells isolated from human foreskin differentiate to form glial cells as assayed by expression of

\*\*\*GFAP\*\*\* and CNP.
FIG. 26 shows that skin-derived stem cells isolated from human foreskin differentiate to form additional neuronal cells types as assayed by expression of \$100 and peripherin. \$100 is a marker of bipolar cells and peripherin is a marker of peripheral neurons.

peripherin is a marker of peripheral neurons. FIG. 27 shows that skin-derived stem cells isolated from human foreskin differentiate to form non-neural cell types as assayed by expression of

smooth muscle actin.

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LOW OXYGEN CULTURING OF CENTRAL NERVOUS SYSTEM PROGENITOR CELLS; GROWTH

OF CELLS IN CULTURE UNDER CONDITIONS THAT PROMOTE CELL SURVIVAL,

PROLIFERATION, AND/ OR CELLULAR DIFFERENTIATION. THE PRESENT INVENTORS

HAVE FOUND THAT PROLIFERATION WAS PROMOTED AND APOPTOSIS REDUCED WHEN

CELLS WERE GROWN IN Csete Marie; Doyle John; McKay Ron; Studer Lorenz; Wold Barbara J California Institute of Technology

National Institutes of Health

(13190, 33614)

PI US 6610540 B1 20030826 AI US 1999-425462 19991022

RLI US 1998-195569 19981118 CONTINUATION-IN-PART 6184035

FI US 6610540 20030826

US 6184035 DT Utility; Granted Patent - Utility, no Pre-Grant Publication

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MRN 010701 MFN: 0440 010701 0468

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FIG. 1. Effect of lowered oxygen on precursor yield in vitro at varying plating densities. Striatal cultures were expanded with \*\*\*bFGF\*\*\* in lowered or ambient oxygen, and total cell numbers assessed after 5 days of proliferation when over 95% of cells are \*\*\*nestin\*\*\* + precursors. Significantly increased cell numbers were detected at all densities in lowered O2 compared to 20% oxygen.

FIG. 2. Lowered oxygen culturing leads to increased proliferation of CNS precursors. FIG. 2A. Mesencephalic precursors were pulsed with 10 mu M BrdU for 60 minutes immediately before fixation, then stained for BrdU uptake. More BrdU+ cells were seen in lowered oxygen cultures during both proliferation and differentiation. Scale bar=20 mu m. FIG. 2B. Mesencephalic precursors in lowered O2 yielded an increased percentage of BrdU+ cells (FIG. 2B-1) and a greater absolute number of BrdU+ cells (FIG. 2B-2) than cultures maintained at 20% O2. Data are given as mean +/-SEM, n=40. Differences between lowered and 20% O2 were statistically significant at all time points and for all parameters (n=8, p less-than 0.05) except percentage of BrdU+ cells at day 4 of expansion (n=8, p=0.10).

Fig. 3. CNS precursors cultured in lowered (vs. 20%) O2 have reduced rates of apoptosis. FIG. 3A. Apoptosis was assayed by TUNEL labeling of

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02. Representative figures of the expansion phase (2 and 6 days of
                                                                                                      ***bFGF***
 culture) and the differentiation phase (4 days after
 withdrawal) are shown. Scale bar=20 mu m. FIG. 3B. Precursors grown at
 lowered 02 showed a significant decrease in the percentage of apoptotic
 cells (n=8, p less-than 0.05) compared to traditional cultures.
FIG. 4. Basic differentiation patterns of CNS stems in lowered and 20% O2 cultures. FIG. 4A. Striatal cultures in lowered or 20% O2 were assessed
 for the relative percentages of precursorderived neurons (by TUJ1 stain), astrocytes ( ***GFAP*** ) and oligodendrocytes (Gal-C) after 5 days of ***bFGF*** proliferation followed by four days of cell differentiation (for quantification see text). FIG. 4B. Passaged mesencephalic precursors
 were proliferated for 6 days and differentiated for 5 days in lowered or
 20% 02 and analyzed for 04, a marker of oligodendrocyte precursors. 04+
 cells could be detected only in lowered oxygen cultures. FIG. 4C.
                             + clones were derived from single passaged mesencephalic
precursor cells after 20 days of ***bFGF*** proliferation (left panel). Clones in lowered oxygen differentiated into TUJ1+ neurons upon ***bFGF*** withdrawal (right panel). FIG. 4D. Lowered O2 promotes clor formation efficiency. The yield of clones derived from single precursors was 3-fold higher in lowered O2 compared to 20% O2 cultures. The majority of clones derived from precursors in O2 oxygen cultures contained 50-500 cells whereas clone size in 20% O2 cultures was generally 5-50 cells (FIG. 4E). Scale bar=20 mu m in all panels
     ***Nestin***
  (FIG. 4E). Scale bar=20 mu m in all panels:
FIG. 5. Lowered O2 culturing improves the yield of functional
 precursor-derived dopaminergic neurons. FIG. 5A and FIG. 5B. Precursors
                                                                                        ***bFGF***
  from E12 mesencephalon were proliferated with
                                                                                                                 for 5 days
 followed by 5 days of differentiation, then stained for the neuronal marker TUJ1 and for TH. A large increase in total number (and percentage) of TH+ neurons was detected (p less-than 0.001) in lowered O2 compared to 20% O2 cultures. Scale bar=20 mu m. FIG. 5C. Quantification of TH protein level by Western blot analysis revealed significantly more TH in samples
  from lowered (vs. 20%) O2 cultures. Each lane was loaded with 2.5 m mu g
  total protein. FIG. 5D. rp-HPLC with electrochemical detection was used
 to quantify dopamine levels in conditioned medium (24 hrs), in HBSS after 15 minutes of conditioning (basal release), and in HBSS+56 mM KCl after 15 minutes (evoked release) (FIG. 5D-1). Significantly more dopamine was detected in cultures maintained at lowered O2 compared to those grown at 20% O2 under all these conditions (conditioned medium p less-than 0.01; basal and evoked release p less-than 0.05) FIG. 5D-2 chows twoice?
 basal and evoked release p less-than 0.05). FIG. 5D-2 shows typical chromatogram for dopamine detection in lowered and 20% 02 cultures.
FIG. 6. Neuronal subtype differentiation from mesencephalic precursors in lowered vs. 20% O2. Double immunocytochemical labeling revealed that
 lowered 02 culturing markedly increased the representation of dopaminergic and serotonergic neuronal (Tuj1+) subtypes, but decreased the representation of GABA+ and Glutamate+ neurons (FIG. 6A). Colony depicted in GABA stain at 20% 02 is an unusual example of very high GABA expression under these conditions. TH and GABA were not co-expressed as
  seen in some developing neurons in vivo. Floor plate cells (FP4+) were
  more numerous in lowered 02 cultures as was the percentage of neurons
  expressing the midbrain transcription factor Enl. Precursor markers
                                and PSA-NCAM were both reduced in lowered 02 cultures
      ***nestin***
  after differentiation compared to 20% O2 conditions (FIG. 6B). Scale
  bars=20 mu m.
FIG. 7. Differential gene expression in mesencephalic precursors at
  lowered and 20% O2 assessed by RT-PCR. FIG. 7A. Expression of genes
  involved in the physiological response to changes in oxygen levels. The
  expression of HIF1 alpha, VHL, EPO and VEGF was assessed after 2 or 6
  days of expansion and after differentiation (day 4 of differentiation=day
  10 of culture) in lowered and 20% O2. Data are normalized to GAPDH
  expression. A significant increase in EPO expression was detected in
  lowered oxygen versus 20% O2 mostly during cell differentiation, whereas VEGF was upregulated during both expansion and differentiation. Surprisingly, no major oxygen-dependent regulation of HIF1 alpha or VHL was observed. FIG. 7B. Candidate genes involved in midbrain development were also tested for O2-dependent differential expression. Increased
  expression of TH and Ptx-3 during cell differentiation confirmed the larger number of functional dopaminergic neurons in lowered oxygen
  cultures (compare FIG. 5). Significant lowered 02-mediated changes in
  expression levels of FGF8 and En1 were also detected.
FIG. 8. EPO mimics the lowered oxygen effect on dopaminergic
  differentiation. Saturating concentrations of EPO or EPO neutralizing
  antibody were added to E12 mesencephalic precursor cultures during both proliferation and differentiation phase (5 days each) in lowered or 20% O2 (FIG. 8A). EPO supplementation significantly increased TH+ cell numbers in 20% O2 cultures (n=6, p less-than 0.05) (FIG. 8B). EPO
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(n=6, p lessthan 0.01) and 20% O2 cultures (n=6, p less-than 0.05) (FIG. 8B) . Scale bar=20 mu m.

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British Columbia, University of CA
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               Monoclonal derivation is confirmed by the presence of a single integrated
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               (A) NSCs tend to grow as clusters in serum-free bFGFsupplemented medium. They differentiate spontaneously into neurofilament-immunoreactive neurons (B) or CNPaseimmunoreactive oligodendrocytes (C) when transferred to serumcontaining medium, or into ***GFAP*** -expressing astrocytes
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                alpha-subunit of beta-hexosaminidase resulting in absence of
               hexosaminidase-A39, were exposed to secreted gene products from human NSCs to assess their ability to effect complementation of the defect. (A-C) Hexosaminidase activity as determined by NASBG histochemistry (Nomarski optics). Functional hexosaminidase produces a red-pink precipitate with an intensity proportional to the level of activity. (A)
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 respectively). A subset of these now alphasubunit-positive corrected cells (D) were neurons, as indicated by their expression of the neuronal marker NeuN (G,J); a subset of the alpha-subunit-cells (E) were glial, as illustrated by their co-expression of the glial marker ***GFAP***

(H,K); and a subset of the alpha-subunit-cells (E) were immature
  (H,K); and a subset of the alpha-subunit+cells (F) were immature, undifferentiated CNS precursors, as indicated by the presence of the intermediate filament ***nestin*** (I,L). (Untreated cells from a subset of the intermediate filament ***nestin***
                                                                                                                             (I,L). (Untreated cells from a
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 (N) Complementation of gene product deficiency results in rescue of a pathologic phenotype in mutated neural cells, as illustrated by percentage of Tay-Sachs CNS cells with diminished GM2 accumulation. Among Tay-Sachs cells not exposed to NSCs (1st histogram), the percentage of GM2+cells was large reflecting their pathologically high level of storage and consistent with a lack of enzyme as per (M). In contrast, the percentage of cross-corrected Tay-Sachs cells without detectable GM2 storage following exposure to murine (2nd and 3rd histograms, as in (M)) or human NSCs (4th histogram) was significantly lower than in the mutant
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FIGS. 4A-4E: Developmentally-appropriate migration of human neural stem cells (NSCs) following engraftment into the subventricular germinal zone (SVZ) of newborn mice. (A,B) Donorderived human NSCs integrate and interminale nondisruptively with endogenous progenitors within the host
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  interspersed with densely packed endogenous SVZ cells, visualized by DAPI (blue) in the overlapping image in (B). (C) Two weeks following transplantation, many donor-derived cells (red) have migrated extensively within the subcortical white matter (arrow) and corpus callosum (c) from their site of implantation in the lateral ventricles (LV), as visualized in this coronal section. A representative migrating cell within the subcortical white matter (arrow), visualized at higher magnification in the boxed insert, is noted to have a leading process characteristic of
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   violet-counterstained parasagittal section, other donor-derived cells
   migrated from their integration site in the anterior SVZ to enter the rostral migratory stream ("RMS") leading to the olfactory bulb ("OB")
   Representative BrdU-immunoperoxidase-positive (brown) donorderived cells (arrow) within the RMS, are seen at low power in (D) and visualized at higher magnification in (E), intermixed with migrating host cells. Further characterization and visualization of these donor human NSC-derived cells in their final location in the OB are presented in FIG.
                                                  100 mu m.
    5. Scale Bars:
 FIGS. 5A-5Q: Differentiation and disseminated foreign gene (
    beta-galactosidase) expression of human neural stem cell (NSC) clones in
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(A-C) Stably engrafted, beta-galactosidase (beta gal)-expressing, donor-derived cells from representative human NSC_clone_H1, detected with
    Xgal histochemistry (A,B) and with anti-beta gal ICC (C). The donor-derived cells pictured in the series of photomicrographs in (A) are within the periventricular and subcortical white matter regions (as per
     FIG. 4). (The top and bottom panels-low power on the left, corresponding high power on the right-are from representative semi-adjacent regions
    within a single recipient, suggesting a significant distribution of cells; arrows indicate the lateral ventricles). Furthermore, as
      illustrated in (B,C) by representative high power photomicrographs through the olfactory bulb (OB) (located as in FIG. 4D), donor-derived cells from this clone have not only migrated extensively to this
      developmentally-appropriate site, but continue to express beta gal in
     this distant location (i.e., in a disseminated fashion in vivo). The normal fate of a subpopulation of SVZderived progenitors that have
     migrated to the OB at this developmental stage is to become neuronal In (D-G), donorderived neurons in the mature OB, derived from BrdU-labeled NSCs (representative clone H6 implanted into the SVZ at birth, are
      identified by both their immunoreactivity to a humanspecific NF antibody
     (D) as well as their expression of the mature neuronal marker, NeuN (E-G); under confocal microscopy, a BrdU+ (hence, donor-derived) cell (arrow in (E), fluorescein) is NeuN+ (arrow in (F), Texas Red) appreciated best with a dual filter (arrow in (G)). Adjacent to this
      representative donorderived BrdU+/NeuN+ neuron (arrow), are 2 host OB
     neurons (BrdU/NeuN+ in (G)) which share a similar size, morphology, and location with the donor-derived cell (arrow in F). (H,I) High power view of a representative donor-derived (clone H6) oligodendrocyte (arrow), appropriately in the adult subcortical white matter (as per FIG. 4C) following neonatal intraventricular implantation, double-labeled with an antibody to the oligodendrocyte-specific protein CNPase (H) and BrdU (I).
      Characteristic cytoplasmic processes extending from the soma are noted (arrowhead in (H)). The morphology of the CNPase+cell has been somewhat damaged by the HCl pre-treatment required for BrdU double-labeling). (J)
      Mature donor-derived astrocytes (clone H6) in the adult subcortical white matter (arrow) (as per FIG. 4C) and striatum following neonatal intraventricular implantation, identified with a human-specific anti-
***GFAP*** antibody. The inset better illustrates at higher magnification the characteristic mature astrocytic market as for the characteristic mature as for the ch
      magnification the characteristic mature astrocytic morphology of a representative human- ***GFAP*** +cell. (K-Q) Expression of vmyc is downregulated within 48 hours following engraftment. (K), (M), and (O) are DAPI-based nuclear stains of the adjacent panels (L), (N), and (P, a
       Q), respectively. Representative human NSC clone H6 was generated (as was
      Q), respectively. Representative numan NSC clone H6 was generated (as was the well-characterized murine NSC clone C17.2) with the propagating gene vmyc. vmyc immunoreactivity in H6-derived cells (red) in the SVZ (arrows) at 24 hours following engraftment ((L) and at higher power in (N)), is persistently absent (P) in integrated H6-derived cells (visualized by BrdU labeling in (Q) (shown here 3 weeks following transplantation, but representative of any point 24 hours after engraftment). Scale Bars: (A), (K) and applies to (L): 100 mu m; (D), (E) and applies to (F,G), (H) and applies to (I), (J), (M) and applies to (N): 10 mu m; ()) and applies to
(P,O): 50 mu m

FIGS. 6A-6J: Neuronal replacement by human neural stem cells (NSCs) following transplantation into the cerebellum of the granule neuron-deficient meander tail (mea) mouse model of neurodegeneration.

(A-G) BrdU-intercalated, donor-derived cells (from representative clone H6) identified in the mature cerebellum by anti-BrdU immunoperoxidase cytochemistry (brown nuclei) following implantation into the neonatal mea external germinal layer (EGL). (The EGL, on the cerebellar surface, disappears as the internal granule layer (IGL) emerges to become the deepest cerebellar cortical layer at the end of organogenesis13) (A) Clone H6-derived cells are present in the IGL ("igl"; arrowheads) of all lobes of the mature cerebellum in this parasagittal section. (Granule neurons are diminished throughout the cerebellum with some prominence in the anterior lobe). (B) Higher magnification of the representative posterior cerebellar lobe indicated by arrowhead "b" in (A), demonstrating the large number of donor-derived cells present within the recipient IGL. (C-G) Increasing magnifications of donor-derived cells (brown nuclei) within the IGL of a mea anterior cerebellar lobe.

(Different animal from that in (A,B).) (G) Normarski optics bring out
         (P,Q): 50 mu m
         (Different animal from that in (A,B).) (G) Normarski optics bring out the similarity in size and morphology of the few residual host,
         BrdU-negative cerebellar granule neurons (arrowheads) and a BrdU+,
        donor-derived neuron (arrow), which is representative of those seen in all engrafted lobes of all animals.) (H,I) Confirmation of the neuronal differentiation of a subpopulation of the donor-derived, BrdU+cells from (A-G) is illustrated by co-labeling with antiBrdU (green in H) and the
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arrows). (Some adjacent, donorderived cells are non-neuronal as indicated by their BrdU+ (arrowhead in (H)) but NeuN-phenotype (also illustrating the specificity of the immunostaining). (J) Cells within the IGL are confirmed to be human donor-derived cells by FISH with a human-specific probe (red) identifying human chromosomal centromeres. Scale Bars: (A), (B): 100 mu m; (F), (G), (J): 10 mu m!

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                                                                                                                                                                                     ***GFĀP***
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NSC-derived cells in their final location in the OB are presented in FIG.
       5. Scale Bars: 100 mu m.
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      within the periventricular and subcortical white matter regions (as per
      FIG. 4). (The top and bottom panels-low power on the left, corresponding high power on the right-are from representative semi-adjacent regions
     within a single recipient, suggesting a significant distribution of cells; arrows indicate the lateral ventricles). Furthermore, as illustrated in (B,C) by representative high power photomicrographs through the olfactory bulb (OB) (located as in FIG. 4D), donor-derived cells from this clone have not only migrated extensively to this developmentally-appropriate site, but continue to express beta gal in this distant location (i.e., in a disseminated fashion in vivo). The normal fate of a subpopulation of SVZderived progenitors that have migrated to the OB at this developmental stage is to become neuronal.
 In (D-G), donor-derived neurons in the mature OB, derived from BrdU-labeled NSCs (representative clone H6) implanted into the SVZ at birth, are identified by both their immunoreactivity to a human-specific NF antibody (D) as well as their expression of the mature neuronal marker, NeuN (E-G); under confocal microscopy, a BrdU+(hence, donor-derived) cell (arrow in (E), fluorescein) is NeuN+(arrow in (F), Texas Red) appreciated best with a dual filter (arrow in (G)). Adjacent to this representative donor-derived BrdU+(NeuN+neuron (arrow)) are 2
       to this representative donor-derived BrdU+/NeuN+neuron (arrow), are 2
       host OB neurons (BrdU-/NeuN+in (G)) which share a similar size,
      morphology, and location with the donor-derived cell (arrow in F). (H,I) High power view of a representative donor-derived (clone H6) oligodendrocyte (arrow), appropriately in the adult subcortical white matter (as per FIG. 4C) following neonatal intraventricular implantation, double-labeled with an antibody to the oligodendrocyte-specific protein
      CNPase (H) and BrdU (I). Characteristic cytoplasmic processes extending from the soma are noted (arrowhead in (H)). (The morphology of the CNPase+cell has been somewhat damaged by the HCl pre-treatment required
       for BrdU double-labeling). (J) Mature donor-derived astrocytes (clone H6)
     in the adult subcortical white matter (arrow) (as per FIG. 4C) and striatum following neonatal intraventricular implantation, identified with a human-specific anti- ***GFAP*** antibody. The inset better illustrates at higher magnification the characteristic mature astrocytic morphology of a representative human- ***GFAP*** +cell. (K-Q) Expression of vmyc is downregulated within 48 hours following engraftment. (K), (M), and (O) are DAPI-based nuclear stains of the adjacent panels (L), (N), and (P, Q), respectively. Representative human NSC clope H6 was generated (as was the well-characterized murine NSC
      NSC clone H6 was generated (as was the well-characterized murine NSC clone C17.2) with the propagating gene vmyc. vmyc immunoreactivity in H6-derived cells (red) in the SVZ (arrows) at 24 hours following engraftment ((L) and at higher power in (N)), is persistently absent (P) in integrated H6-derived cells (visualized by BrdU labeling in (Q) (shown the result of t
  here 3 weeks following transplantation, but representative of any point 24 hours after engraftment). Scale Bars: (A), (K) and applies to (L): 100 mu m; (D), (E) and applies to (F,G), (H) and applies to (I), (J), (M) and applies to (N): 10 mu m; (O)) and applies to (P,Q): 50 mu m FIGS. 6A-6J: Neurolantation to the proposed statement by human neural stem cells (NSCs)
     FIGS. 6A-6J: Neuronal replacement by human neural stem cells (NSCs) following transplantation into th cerebellum of the granule neuron-deficient meander tail (mea) mouse model of neurodegeneration. (A-G) BrdU-intercalated, donor-derived cells (from representative clone H6) identified in the mature cerebellum by anti-BrdU immunoperoxidase cytochemistry (brown nuclei) following implantation into the neonatal mea external germinal layer (EGL). (The EGL, on the cerebellar surface, disappears as the internal granule layer (IGL) emerges to become the deepest cerebellar cortical layer at the end of organogenesis13) (A) Clone H6-derived cells are present in the IGL ("igl"; arrowheads) of all lobes of the mature cerebellum in this parasagittal section. (Granule neurons are diminished throughout the cerebellum with some prominence in
       neurons are diminished throughout the cerebellum with some prominence in the anterior lobe). (B) Higher magnification of the representative posterior cerebellar lobe indicated by arrowhead "b" in (A), demonstrating the large number of donor-derived cells present within the recipient IGL. (C-G) Increasing magnifications of donor-derived cells
        (brown nuclei) within the IGL of a mea anterior cerebellar lobe. (Different animal from that in (A,B).) (G) Normarski optics bring out the similarity in size and morphology of the few residual host,
```

donor-derived neuron (arrow), which is representative of those seen in all engrafted lobes of all animals.) (H,I) Confirmation of the neuronal differentiation of a subpopulation of the donor-derived, BrdU+cells from (A-G) is illustrated by co-labeling with antiBrdU (green in H) and the mature neuronal marker NeuN (red in I) (indicated with corresponding arrows). (Some adjacent, donorderived cells are non-neuronal as indicated by their BrdU+(arrowhead in (H)) but NeuN-phenotype (also illustrating the specificity of the immunostaining). (J) Cells within the IGL are confirmed to be human donor-derived cells by FISH with a human-specific probe (red) identifying human chromosomal centromeres. Scale Bars: ((A), (B): 100 mu m; (F), (G), (J): 10 mu m!

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DUPLICATE 28
       ANSWER 60 OF 313 USPATFULL on STN
L5
          2003:51551 USPATFULL
AN
          TGF-alpha polypeptides, functional fragments and methods of use therefor
TI
          Twardzik, Daniel R., Bainbridge Island, WA, UNITED STATES
Pernet, Andre, Lake Forest, IL, UNITED STATES
Felker, Thomas S., Vashon, WA, UNITED STATES
Paskell, Stefan, Bainbridge Island, WA, UNITED STATES
Reno, John M., Brier, WA, UNITED STATES
IN
                                     Αĺ
                                             20030220
          US 2003036509
PI
                                             20040113
          US 6677307
                                     B2
          US 2002-138158 A1 20020501 (10)
Continuation-in-part of Ser. No. US 2000-641587, filed on 17 Aug 2000,
PENDING Continuation-in-part of Ser. No. US 2000-559248, filed on 26 Apr 2000, PENDING Continuation-in-part of Ser. No. US 1999-459813, filed on 13 Dec 1999, PENDING Continuation-in-part of Ser. No. US 1999-378567, filed on 19 Aug 1999, ABANDONED
ΑI
RLI
DT
          Utility
          APPLICÁTION
FS
LN.CNT
          2915
INCL
          INCLM: 514/012.000
          INCLS: 530/399.000
                    514/012.000
NCL
          NCLM:
          NCLS:
                    530/300.000; 530/402.000
IC
          [7]
          ICM: A61K038-18
          ICS: C07K014-475
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       ANSWER 61 OF 313
                                CAPLUS
                                             COPYRIGHT 2004 ACS on STN
AN
       2003:154584 CAPLUS
DN
       138:201346
TI
       Generation of multipotent central nervous system stem cells
       U, Hoi Sang
IN
       Regents of the University of California, USA
PA
       PCT Int. Appl., 62 pp.
SO
       CODEN: PIXXD2
DT
       Patent
LΑ
       English
FAN.CNT 1
                                    KIND
                                               DATE
                                                                APPLICATION NO.
                                                                                                  DATE
       PATENT NO.
                                     _ - - -
                                                                                                  20020323
       WO 2003016507
                                     A2
                                               20030227
                                                                WO 2002-US9160
PI
       WO 2003016507
                                      Α3
                                               20030515
                   AE, AG, AL, AM, AT, AU, AZ,
                                                            BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             W:
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                   CO, CR, CU,
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                                    ID, IL, IN, IS, JP,
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                                                                                         KZ, LC, LK, LR,
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                                    LV,
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                                                                                                     OM, PH,
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                                                                                         NO,
                                          MA, MD, MG, MK,
                                                                  MN, MW, MX, MZ,
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                               LU,
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                                                                  SK,
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                                    RU,
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                                                                                         TN, TR,
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                               RO,
                                          VN, YU, ZA,
                                                            ZM,
                                                                  ZW, AM, AZ, BY,
                                                                                         KG, KZ,
                              US, UZ,
                   UA, UG,
                   TJ,
                         TM
                   GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, 278510P P 20010323
                                                                                                     BE,
                                                                                                           CH,
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                                                                                                      TD,
PRAI US 2001-278510P
                                             COPYRIGHT 2004 IFI on STN
L_5
       ANSWER 62 OF 313
                                  IFIPAT
                       IFIPAT; IFIUDB; IFICDB
AN
         LONG-TERM CELL-CULTURE COMPOSITIONS AND GENETICALLY MODIFIED ANIMALS
TI
         DERIVED THEREFROM; ISOLATING, CULTURING AND PROPAGATING FETAL NEURAL STEM CELLS FOR GENE TARGETING AND GENE KNOCKOUT EXPERIMENTS AND FOR NUCLEAR
         TRANSFER EXPERIMENTS
         Hayes Eric Shannon (CA); Lacham-Kaplan Orly (AU); Morrison John Roderick (AU); Pera Martin Frederick (AU); Trounson Alan Osborne (AU)
IN
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US 2003143737
                                                      20030731
            US 2000-732520
                                                      20001207
AI
PRAI
            AU 1999-4495
                                                      19991207
            AU 2000-9242
                                                      20000807
            AU 2000-1108
                                                      20001031
            AU 2000-1109
                                                      20001031
            US 2003143737
FI
                                                      20030731
            Utility; Patent Application - First Publication
DT
            CHEMICAL
FS
            APPLICATION
CLMN
GΙ
              11 Figure(s).
          FIG. 1 shows the neural stem cells form a multilayered culture displaying
            a number of morphologies depending on whether the cells are in direct
          contact with the tissue culture plate or are part of a secondary layer (FIG. 1A). Continued proliferation of the cells results in the formation of budding structures (FIG. 1B), which will eventually "hatch" generating balls of cells floating in the media. These balls can be cultured in suspension or disaggregated to for growing on tissue culture plates.

FIG. 2 shows that the cells are positive for a number of markers consistent with neural stem cells including ***nestin*** (FIG. 2A)
             and vimentin (FIG. 2B).
           FIG. 3 shows A) B) phase contract images of FNS cells that have been
            allowed to differentiate by passaging at low density. The cells are
            positive for markers of differentiated neuronal stem cells. C) shows
             differentiated neuronal stem cells expressing
                                                                                                                  ***GFAP***
                                                                                                                                               which is a
            marker of glial cells, using immunofluorescence. D) shows differentiated
             cells expressing beta-tubulin a marker consistent with neurones using
             immunofluorescence
           FIG. 4 shows the effect of ***bFGF***
                                                                                                  (FGF2) on FNS cell
                                                  ***bFGF***
                                                                           ranging in concentration from 0-50 ng/ml
             proliferation.
             was applied to various passage FNS cells (ie passage 2-12). At early
             passage number the cells show some independence of added growth factors
           which is lost past passage #5. Optimal ***bFGF*** stimulated proliferation of FNS cells occurs at approximately 5 ng/ml.

FIG. 5 shows the effect of ***EGF*** on FNS cell proliferation,

***EGF*** ranging in concentration from 0-50 ng/ml was applied to
            various passage FNS cells (ie passage 2-12). At early passage number the cells show some independence of added growth factors which is lost past
                                                         ***bFGF***
             passage #5. Optimal
                                                                                      stimulated proliferation of FNS cells
             occurs at approximately 5 ng/ml.
                                                                                                                                 ***bFGF***
           FIG. 6 shows the combined effect of
                                                                                          ***EGF***
                                                                                                                   and
             FNS cell proliferation: A) Low concentration and B) high concentration. The combined effect of ***EGF*** and ***bFGF*** was tested on F
             The combined effect of
                                                                                                                                  was tested on FNS
            cells. An optimal concentration of 2-5 ng/ml was observed for each growth factor when used in combination.
FIG. 7 shows long-term culture of FNS cells in the presence of and absence of the ECE that the presence of the ECE that the ECE that the presence of the ECE that the presence of the ECE that the EC
                       ***EGF*** or ***bFGF*** . While there appears to be some
             variation between the various passages it was generally noted that there
             was little added benefit to adding both over adding ***bFGF*** alone to the
                                                                                                     ***EĞF***
                                                                                                                              and
                                                                                                                                           ***bFGF***
                                                                    alone to the culture system. However the FNS sponsive to ***EGF*** in the early
             cells appear to be more responsive to
             passages.
           FIG. 8 shows the effect of lipid on the propagation of foetal neural stem
             cells. All cells were propagated in the standard Neurobasal A media (with
             supplements) in the presence or absence of the Chemically defined lipid concentrate (diluted 1:100).
           FIG. 9 shows the characteristics of cells grown in either DMEM/ F12 media
             or Neurobasal A (plus supplements) media with or without the addition of
            the chemically defined lipid supplement. A) DMEM/F12-lipid (10 x magnification); B) DMEM/F2-lipid (32 x magnification); C) DMEM/F12+lipid (10 x magnification); D) DMEM/F12+lipid (20 x magnification); E) Neurobasal A-lipid (10 x magnification); F) Neurobasal A-lipid (32 x magnification); G) Neurobasal A+lipid (10 x magnification); H) Neurobasal A-lipid (20 x magnification)
             A+lipid (20 x magnification)
           FIG. 10 shows assessment of FNS cell proliferation using BrdU
             incorporation at 160 x magnification. A) and C) shows BrdU incorporation
             into passage #2 and passage #17 cells, respectively; BrdU incorporation is visualised using an mouse monoclonal anti-BrdU (Sigma) in combination
             with FITC conjugated goat anti-mouse. Photos are paired-there is one shot
             of BrdU immunofluorescence A) and C), and one shot of the same cells
             using phase contrast microscopy B) and D).
           FIG. 11 shows the histology of tumours formed by the injection of PC12 cells (a neuronal cell tumour line) into SCID mice. Tissues were
             collected 19 days after injection and stained with H&E. The tumour
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cells (passage # 12) failed to display any signs of tumour formation after 13 weeks.

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ANSWER 63 OF 313 IFIPAT COPYRIGHT 2004 IFI on STN
L5
                           IFIPAT; IFIUDB; IFICDB
AN
           BONE MARROW CELLS AS A SOURCE OF NEURONS FOR BRAIN AND SPINAL CORD
TI
           REPAIR; BONE-MARROW DERIVED NEURONAL CELLS FOR USE IN THE TREATMENT OF
           NERVOUS SYSTEM DISORDERS
           Freeman Thomas; Janssen William; Sanberg Paul; Sanchez-Ramos Juan; Song
IN
           Shijie
           South Florida, University of (16948)
PA
                                               20030304
PΙ
           US 6528245
                                      В2
                                      A1
           US 2002146821
                                               20021010
           US 1999-307824
                                               19990507
AΙ
           US 1998-84533P
                                              19980507 (Provisional)
PRAI
                                                                (Provisional)
           US 1998-112979P
                                              19981217
                                              19990416
                                                               (Provisional)
           US 1999-129684P
           US 6528245
US 2002146821
                                               20030304
FI
                                               20021010
           Utility
DT
           CHEMICĀL
FS
           GRANTED
           010150
                          MFN: 0426
MRN
           011898
                                    0610
                                    0446
           012219
CLMN
         9 Drawing Sheet(s), 32 Figure(s).
FIG. 1 is a bar graph. BMSC adherent to culture dishes were treated with
***EGF*** (10 ng/ml), RA (0.5 mu M) or RA plus BDNF (10 ng/ml) for 7
days. Each bar represents the mean number (+-SEM) of fibronectin
GΙ
           immunoreactive cells per visual field (20 x objective) determined in 20 fields per dish in 4 culture dishes. *=p less-than 0.05, two-tailed
           t-test
         FIGS. 2A through 2F are photomicrographs of BMSC from lacZ mice that have been co-cultured with mouse fetal midbrain cells for 2 weeks in N5 medium supplemented with cis-9 retinoic acid (0.5 mu M) and BDNF (10 ng/ml). FIGS. 3A through 3F are photomicrographs, which illustrate the migration and integration of BMSC into rat midbrain. FIG. 3A (scale bar=500 mu m) shows symmetrical distribution despite unilateral grafting into the striatum. FIG. 3B is a region of the paraventricular nucleus (scale)
           striatum. FIG. 3B is a region of the paraventricular nucleus (scale
           bar=100 mu m). None of the beta-gal+cells are labeled with the red-brown
           stain (TH-ir). FIGS. 3A (Scale bar=500 mu m), 3B (Scale bar=100 mu m) and
           3C (Scale bar=50 mu m) depict cells doubly stained for beta-gal and TH-ir. FIGS. 3D (Scale bar=50 mu m) and 3E (Scale bar=25 mu m) illustrate sections from the red nucleus that have doubly stained for beta-gal and NeuN-ir. FIG. 3F (Scale bar=25 mu m) illustrates beta-gal+cells from the
           red nucleus also doubly stained for MAP2-ir.
          FIGS. 4A through 4F are photomicrographs of a section from rat cerebellar
           lobule illustrating laminar distribution of betagal+cells in a
           distribution of Purkinje cells. beta-gal+are colabeled with calbindin immunoreactivity in FIGS. 4A, 4B, and 4C. (Scale bar=100 mu m in 4A, 50 mu m in 4B and 25 mu m in 4C). FIG. 4D shows beta-gal+Purkinje cells co-labeled with GAD-ir (Scale bar=50 mu m). FIG. 4E illustrates dense MAP2-ir fibers enveloping beta-gal+Purkinje cells (Scale bar=25 mu m). FIG. 4F illustrates beta-gal+cells co-labeled with NeuN-ir in the deep cerebellar nucleus (Scale bar=25 mu m).
          FIGS. 5A through 5D are photomicrographics showing the production of
           markers for fibronectin (FIG. 5A) and differentiated BMSC with nerve cell
         markers (FIGS. 5B, 5C and 5D).

FIG. 6 is a Western blot of the lysates of BMSC conditioned with four different treatments and labeled with ***GFAP*** -ir, ***nesting and Neun. BDNF+RA+N5 induced the strongest expression of nerve cell and Neun. BDNF+RA+N5 induced the strongest expression of nerve cell and Neun.
           markers while glial cell markers was most strongly expressed after N5
           alone.
          FIGS. 7A through 7F are photomicrographs of human BMSC which were co-cultured with fetal rat striatal cells in N5 formulation with BDNF+RA.
           These figures show that human BMSC (green labeled in FIGS. 7C and 7D and yellow in FIGS. 7E and 7F) can be induced to express neural markers NeuN
                                                       ***GFAP***
                                                                                (FIGS. 7B and 7F).
            (FIGS. 7A and 7E)
                                             and
          FIG. 8 is a photomicrograph of rat brain, showing that mouse BMSC labeled
           with red PKH26 also express the neuron marker NeuNir (green fluorescence). In addition, the morphology of the doubly labeled cells is
            that of neurons.
          FIG. 9 is a photomicrograph of rat brain, showing a doubly labelled glial
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cell. The red fluorescent tracer identifies it as derived from a BMSC,

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morphology is that of a glial cell.
                           USPATFULL on STN
L5
      ANSWER 64 OF 313
        2003:324321 USPATFULL
AN
        Use of human neural stem cells secreting GDNF for treatment of
TΙ
        parkinson's and other neurodegenerative diseases
        Svendsen, Clive N., Madison, WI, UNITED STATES
IN
        US 2003228295
                                     20031211
                               A1
PI
        US 2003-423710
                                     20030425 (10)
                               A1
AΙ
                               20020425 (60)
        US 2002-375587P
PRAI
        Utility
DT
        APPLICÂTION
FS
LN.CNT
        736
        INCLM: 424/093.210
INCL
        INCLS: 435/368.000
                 424/093.210
NCL
        NCLM:
                 435/368.000
        NCLS:
         [7]
IC
        ICM: A61K048-00
        ICS: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 65 OF 313
                          USPATFULL on STN
L5
        2003:318230 USPATFULL
ΑN
        Myelination of congenitally dysmyelinated forebrains using
TI
        oligodendrocyte progenitor cells
Goldman, Steven A., South Salem, NY, UNITED STATES
Roy, Neeta Singh, New York, NY, UNITED STATES
Windrem, Martha, New York, NY, UNITED STATES
US 2003223972 Al 20031204
US 2003-368810 Al 20030214 (10)
IN
PΙ
AΙ
                                20020215 (60)
        US 2002-358006P
PRAI
DT
        Utility
        APPLICATION
LN.CNT
        1308
         INCLM: 424/093.210
INCL
        INCLS: 435/368.000; 435/456.000; 435/459.000; 435/458.000
NCLM: 424/093.210
NCL
                 435/368.000; 435/456.000; 435/459.000; 435/458.000
        NCLS:
         [7]
IC
         ICM: A61K048-00
         ICS: C12N005-08; C12N015-86; C12N015-88; C12N015-87
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 66 OF 313 USPATFULL on STN
L5
         2003:300379 USPATFULL
AN
         Reprogramming cells for enhanced differentiation capacity using
TI
         pluripotent stem cells
         Earp, David J., Oakland, CA, UNITED STATES
TN
         Carpenter, Melissa K., Castro Valley, CA, UNITED STATES
        Gold, Joseph D., San Francisco, CA, UNITED STATES
Lebkowski, Jane S., Portola Valley, CA, UNITED STATES
Schiff, J. Michael, Menlo Park, CA, UNITED STATES
         US 2003211603
                                      20031113
                               A1
PΙ
         US 2003-344680
WO 2001-US25493
                                      20030212 (10)
                                A1
ΑI
                                      20010814
DT
         Utility
         APPLICATION
FS
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        1597
INCL
         INCLM: 435/366.000
NCL
         NCLM:
                 435/366.000
IC
         [7]
         ICM: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
                            USPATFULL on STN
       ANSWER 67 OF 313
L5
         2003:299866 USPATFULL
AN
         Neutral progenitor cells from hippocampal tissue and a method for
TI
         isolating and purifying them
         Goldman, Steven A., South Salem, NY, UNITED STATES
IN
                                A1
                                      20031113
PΙ
         US 2003211087
                                                 (10)
                                      20021023
ΑI
         US 2002-181329
                                Α1
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20010118

WO 2001-US1780

APPLICATION

Utility

DT FS

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INCL
        INCLM: 424/093.210
        INCLS: 435/368.000; 435/456.000
                424/093.210
NCL
        NCLM:
                435/368.000; 435/456.000
        NCLS:
IC
        [7]
        ICM: A61K048-00
        ICS: C12N005-08; C12N015-861
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
     ANSWER 68 OF 313
                          USPATFULL on STN
ΑN
        2003:288603
                      USPATFULL
        13 human colon and colon cancer associated proteins
TI
        Rosen, Craig A., Laytonsville, MD, UNITED STATES
Birse, Charles E., North Potomac, MD, UNITED STATES
IN
        Human Genome Sciences, Inc., Rockville, MD (U.S. corporation) US 2003203361 A1 20031030
PA
PΙ
        US 2001-997003
                                               (9)
AΙ
                              A1
                                    20011130
        Continuation-in-part of Ser. No. WO 2000-US22157, filed on 11 Aug 2000,
RLI
        PENDING
                               19990813 (60)
PRAI
        US 1999-148680P
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        APPLICĀTION
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INCL
                435/007.230; 435/069.300; 435/183.000; 435/320.100; 435/325.000;
        INCLS:
                536/023.200
NCL
        NCLM:
                435/006.000
                435/007.230; 435/069.300; 435/183.000; 435/320.100; 435/325.000;
        NCLS:
                536/023.200
TC
        [7]
        ICM: C12Q001-68
        ICS: G01N033-574; C07H021-04; C12N009-00; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 69 OF 313
                          USPATFULL on STN
L5
        2003:283103 USPATFULL
ΑN
        Enhancing neurotrophin-induced neurogenesis by endogenous neural
TТ
        progenitor cells by concurrent overexpression of brain derived
        neurotrophic factor and an inhibitor of a pro-gliogenic bone
        morphogenetic protein
        Goldman, Steven A., South Salem, NY, UNITED STATES Chmielnicki, Eva, New York, NY, UNITED STATES Economides, Aris, Tarrytown, NY, UNITED STATES
IN
                                    20031023
        US 2003199447
PI
                              A1
                                    20030214
                                               (10)
        US 2003-368809
                              A1
ΑI
                               20020215 (60)
PRAI
        US 2002-358005P
        Utility
DT
FS
        APPLICATION
LN.CNT
        1728
INCL
        INCLM: 514/012.000
                514/044.000; 424/093.200
        INCLS:
                514/012.000
NCL
        NCLM:
                514/044.000; 424/093.200
        NCLS:
TC
        [7]
        ICM: A61K048-00
        ICS: A61K038-18
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 70 OF 313
                          USPATFULL on STN
        2003:258639
                      USPATFULL
AN
TI
        207 human secreted proteins
        Ni, Jian, Germantown, MD, UNITED STATES
IN
        Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
        LaFleur, David W., Washington, DC,
                                                 UNITED STATES
        Moore, Paul A., Germantown, MD, UNITED STATES
        Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
        Rosen, Craig A., Laytonsville, MD, UNITED STATES
        Ruben, Steven M., Olney, MD, UNITED STATES
        Soppet, Daniel R., Centreville, VA, UNITED STATES
        Young, Paul E., Gaithersburg, MD, UNITED STATES
Shi, Yanggu, Gaithersburg, MD, UNITED STATES
Florence, Kimberly A., Rockville, MD, UNITED STATES
        Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Florence, Charles, Rockville, MD, UNITED STATES
        Hu, Jing-Shan, Mountain View, CA, UNITED STATES
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Kyaw, Hla, Frederick, MD, UNITED STATES
        Fischer, Carrie L., Burke, VA, UNITED STATES
        Ferrie, Ann M., Painted Post, NY, UNITED STATES
        Fan, Ping, Potomac, MD, UNITED STATES
        Feng, Ping, Gaithersburg, MD, UNITED STATES
        Endress, Gregory A., Florence, MA, UNITED STATES
Dillon, Patrick J., Carlsbad, CA, UNITED STATES
Carter, Kenneth C., North Potomac, MD, UNITED STATES
Brewer, Laurie A., St. Paul, MN, UNITED STATES
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AN
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       Human embryoid body-derived cells
       Shamblott, Michael J.,
                               Baltimore,
IN
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                                                UNITED STATES
                  John D., Baltimore, MD,
                                            UNITED STATES
       Gearhart.
       US 2003175954
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TI
       Methods and compositions for producing neural progenitor cells
                       V.,
                            Bethesda, MD, UNITED STATES
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       Agoston, Denes
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AN
        Method for inducing differentiation of embryonic stem cells into
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IN
        Inoue, Kazutomo, Sakyo-ku, JAPAN
        Kim, Dohoon, Sakyo-ku, JAPAN
Gu, Yanjun, Sakyo-ku, JAPAN
        Ishii, Michiyo, Kamigyo-ku,
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AN
TI
        Cultures, products and methods using stem cells
        Weiss, Mark L., Manhattan, KS, UNITED STATES
IN
        Troyer, Deryl L., Manhattan, KS, UNITED STATES Davis, Duane, Westmoreland, KS, UNITED STATES
        Mitchell, Kathy E., Manhattan, KS, UNITED STATES
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        Kansas State University Research Foundation (U.S. corporation)
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        Pluripotent embryonic-like stem cells, compositions, methods and uses
TI
        Young, Henry E., Macon, GA, UNITED STATES
Lucas, Paul A., Poughkeepsie, NY, UNITED STATES
US 2003161817 A1 20030828
US 2001-820320 A1 20010328 (9)
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         Human embryonic germ cell line and methods of use
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         Gearhart, John D., Baltimore, MD, UNITED STATES
Shamblott, Michael Joseph, Baltimore, MD, UNITED STATES
THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE (U.S. corporation)
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         US 1997-989744, filed on 12 Dec 1997, GRANTED, Pat. No. US 6331406
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AN
         Neural transplantation using pluripotent neuroepithelial cells Sinden, John, London, UNITED KINGDOM Gray, Jeffrey A., London, UNITED KINGDOM
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IN
         Hodges, Helen, London, UNITED KINGDOM
         Kershaw, Timothy, London, UNITED KINGDOM
         Rashid-Doubell, Fiza, Oxford, UNITED KINGDOM
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AN
ΤI
         Method of isolating ependymal neural stem cells
         Frisen, Jonas, Stockholm, SWEDEN
IN
         Janson, Ann Marie, Stockholm, SWEDEN
         Johansson, Clas, Stockholm, SWEDEN
         Momma, Stefan, Spanga, SWEDEN
Clarke, Diana, Stockholm, SWEDEN
         Zhao, Ming, Solna, SWEDEN
         Lendahl, Urban, Sundbyberg, SWEDEN
Delfani, Kioumars, Solna, SWEDEN
US 2003129747 Al 20030710
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AN
         Compositions and methods for isolation, propagation, and differentiation
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         of human stem cells and uses thereof
        Neuman, Toomas, Santa Monica, CA, UNITED STATES
Levesque, Michel, Beverly Hills, CA, UNITED STATES
US 2003118566 A1 20030626
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AN
         Pluripotent stem cells derived without the use of embryos or fetal
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         Levanduski, Mike, River Vale, NJ, UNITED STATES US 2003113910 A1 20030619
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 82 OF 313 USPATFULL on STN
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         2003:159428 USPATFULL
AN
         Lineage restricted glial precursors from the central nervous system
TI
         Rao, Mahendra S., Salt Lake City, UT, UNITED STATES Noble, Mark, Brighton, NY, UNITED STATES
IN
         Mayer-Proschel, Margot, Pittsford, NY, UNITED STATES
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AN
         Enriched central nervous system stem cell and porgenitor cell
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         Buck, David W., Heathfield, UNITED KINGDOM
IN
         Uchida, Nobuko, Palo Alto, CA, UNITED STATES
Weissman, Irving, Redwood City, CA, UNITED STATES
         US 2003109039
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        Multi-lineage directed induction of bone marrow stromal cell
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        Black, Ira B., Skillman, NY, UNITED STATES Woodbury, Dale, Piscataway, NJ, UNITED STATES
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AN
        Screening small molecule drugs using neural cells differentiated from
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        human embryonic stem cells
        Carpenter, Melissa K., Castro Valley, CA, UNITED STATES Denham, Jerrod J., San Francisco, CA, UNITED STATES Inokuma, Margaret S., San Jose, CA, UNITED STATES Thies, R. Scott, Pleasanton, CA, UNITED STATES
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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AN
         Ependymal neural stem cells and method for their isolation
TI
         Janson, Ann Marie, Stockholm, SWEDEN Frisen, Jonas, Stockholm, SWEDEN
IN
         Johansson, Clas, Stockholm, SWEDEN
         Momma, Stefan, Spinga, SWEDEN
         Clarke, Diana, Cambridge, MA, UNITED STATES
         Zhao, Minq, Solna, SWEDEN
         Lendahl, Ŭrban, Stockholm, SWEDEN
         Delfani, Kioumars, Solna, SWEDEN
         NeuroNova AB
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TI
                       METHOD FOR NEURAL STEM CELL DIFFERENTIATION USING 5HT1A AGONISTS
                    Rajan , Prithi , Dr., 106 Lynch Street, Rockville, Maryland, UNITED
IN
                    STĂTES
                                           20850
                    Altar , C. Anthony , Mr., 1110 Kenilworth Avenue, Garrett Park, Maryland, UNITED STATES 20896
                    Psychiatric Genomics, Inc., Gaithersburg, 20878, UNITED STATES, Maryland
PA
                     (U.S. corporation)
                                                                                           20030501
                    US 2003082802
                                                                            A1
PI
                    US 2002-175360
                                                                                           20020618 (10)
                                                                            A1
AI
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PRAI
                    US 2001-60299152
DT
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LN.CNT
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NCLS: 514/001.000
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                     ICM: C12N005-08
                     ICS: C12Q001-68; A61K031-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
              ANSWER 88 OF 313
                                                                USPATFULL on STN
L5
                     2003:120030 USPATFULL
AN
TI
                     Methods of screening biological agents
                    Weiss, Samuel, Alberta, CANADA
IN
                    Reynolds, Brent, Alberta, CANADA
Hammang, Joseph P., Barrington, RI, UNITED STATES
Baetge, E. Edward, Barrington, RI, UNITED STATES
PI
                    US 2003082515
                                                                           A1
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                                                                            A1
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ΑI
                    US 2002-199189
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                    ABANDONED Continuation of Ser. No. US 1992-961813, filed on 16 Oct 1992, ABANDONED Continuation-in-part of Ser. No. US 1991-726812, filed on 8
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                     of Ser. No. US 1991-726812, filed on 8 Jul 1991, ABANDONED
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                    Jul 1991, ABANDONED Continuation-in-part of Ser. No. US 1991-726812, filed on 8 Jul 1991, ABANDONED Continuation-in-part of Ser. No. US 1994-311099, filed on 23 Sep 1994, ABANDONED Continuation-in-part of Ser. No. US 1991-726812, filed on 8 Jul 1991, ABANDONED Continuation-in-part of Ser. No. US 1994-338730, filed on 14 Nov 1994, ABANDONED Continuation-in-part of Ser. No. US 1991-726812, filed on 8 Jul 1991, ABANDONED Utility
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                                         435/368.000
IC
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                     ICM: C12Q001-00
                      ICS: C12N005-08
CAS
          INDEXING IS AVAILABLE FOR THIS PATENT.
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L5 ANSWER 89 OF 313 USPATFULL on STN

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Adipose-derived stem cells and lattices
TΙ
       Hedrick, Marc H., Encino, CA, UNITED STATES
IN
       Katz, Adam J., Charlottesville, VA, UNITED STATES
       Llull, Ramon, Mallorca, SPAIN
       Futrell, J. William, Pittsburgh, PA, UNITED STATES
Benhaim, Prosper, Encino, CA, UNITED STATES
Lorenz, Hermann Peter, Belmont, CA, UNITED STATES
        Zhu, Min, Los Angeles, CA, UNITED STATES
       US 2003082152
                                  20030501
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PI
       US 2001-952522
                            A1
                                  20010910 (9)
AΙ
        Continuation-in-part of Ser. No. WO 2000-US6232, filed on 10 Mar 2000,
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       US 1999-123711P
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       US 1999-162462P
                              19991029 (60)
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L5
        2003:113090 USPATFULL
AN
                         -expressing hair follicle stem cells
          ***Nestin***
TI
        Li, Lingna, San Diego, CA, UNITED STATES
IN
        Yang, Meng, San Diego, CA, UNITED STATES
        US 2003077823
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PΙ
        US 2002-251657
US 2001-323963P
                                   20020920
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     ANSWER 91 OF 313 USPATFULL on STN
L5
                     USPATFULL
        2003:86333
AN
        Trans-differentiation and re-differentiation of somatic cells and
TI
        production of cells for cell therapies
        Page, Raymond, Southbridge, MA, UNITED STATES
IN
        Dominko, Tanja, Southbridge, MA, UNITED STATES
                 Christopher, Hudson, MA, UNITED STATES
        Malcuit,
        US 2003059939
US 2002-228296
US 2001-314654P
Utility
                           A1
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PI
                                   20020827
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ΑI
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                435/368.000; 435/372.000
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 92 OF 313
                          USPATFULL on STN
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AN
        2003:79048
        Methods and compositions for the repair and/or regeneration of damaged
TI
        myocardium
        Anversa, Piero, New York, NY, UNITED STATES
IN
                                   20030320
        US 2003054973
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PI
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ΑI
        US 2002-162796
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        Continuation-in-part of Ser. No. US 2001-919732, filed on 31 Jul 2001,
RLI
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                               20010606
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L5
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                   2003:71552
AN
                   In vitro and in vivo proliferation and use of multipotent neural stem
TI
                    cells and their progeny
                   Weiss, Samuel, Alberta, CANADA
TN
                   Reynolds, Brent, Alberta, CANADA
                   Hammang, Joseph P., Barrington, RI, UNITED STATES Baetge, E. Edward, Barrington, RI, UNITED STATES
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  CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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  AN
                     2003:70949 USPATFULL
                    DISCOVERY, LOCALIZATION, HARVEST, AND PROPAGATION OF AN FGF2 AND
  TI
                    BDNF-RESPONSIVE POPULATION OF NEURAL AND NEURONAL PROGENITOR CELLS IN
                    THE ADULT HUMAN FOREBRAIN
GOLDMAN, STEVEN A., SOUTH SALEM, NY, UNITED STATES
NEDERGAARD, MAIKEN, SOUTH SALEM, NY, UNITED STATES
  IN
                                                                    A1
                                                                                      20030313
                     US 2003049234
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                      ICM: A61K048-00
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ANSWER 95 OF 313 USPATFULL on STN
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        2003:57546
                     USPATFULL
AN
        Differentiated cells suitable for human therapy
TI
       Gold, Joseph D., San Francisco, CA, UNITED STATES Lebkowski, Jane S., Portola Valley, CA, UNITED STATES US 2003040111 A1 20030227
IN
PI
                                    20020507 (10)
        US 2002-141220
                             Α1
AI
        Division of Ser. No. US 2001-783203, filed on 13 Feb 2001, PENDING
RLI
        Continuation of Ser. No. WO 2001-US44309, filed on 26 Nov 2001, UNKNOWN
                             20001127 (60)
PRAI
        US 2000-253443P
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        US 2000-253357P
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 96 OF 313
2003:44877 USP
                          USPATFULL on STN
L5
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AN
        Selective antibody targeting of undifferentiated stem cells
ΤI
        McWhir, Jim, Midlothian, UNITED KINGDOM
IN
        Gold, Joseph D., San Francisco, CA, UNITED STATES
        Schiff, J. Michael, Menlo Park, CA, UNITED STATES
                                    20030213
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        US 2003032187
        US 2001-995419
                             Α1
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ΑI
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US 2000-253395P
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                435/366.000
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        ICS: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 97 OF 313
                         USPATFULL on STN
        2003:44871 USPATFULL
AN
TI
        Production of radial glial cells
        Weiss, Samuel, Calgary, CANADA
IN
        Gregg, Christopher, Calgary, CANADA
Stem Cell Therapeutics Inc., Calgary, AB, CANADA (non-U.S. corporation)
PΑ
        US 2003032181
                                    20030213
PI
                              Α1
        US 2002-196549
                                    20020717
AΙ
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                               20011130
PRAI
        CA 2001-2364095
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 98 OF 313 USPATFULL on STN
                     USPATFULL
AN
        2003:44341
        Methods and reagents for cell transplantation
TI
        Lee, Ike W., Norwood, MA, UNITED STATES
TN
        Liu, Guizhen, Norwood, MA, UNITED STATES
Hampe, James, Dedham, MA, UNITED STATES
Croissant, Jeffrey D., Scituate, MA, UNITED STATES
                                    20030213
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PΙ
        US 2003031651
                                    20020412 (10)
        US 2002-121501
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AΙ
                               20010413 (60)
PRAI
        US 2001-283837P
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NCL
        NCLM:
                435/366.000
        NCLS:
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        ICM: A61K045-00
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CAS
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L_5
      ANSWER 99 OF 313
                          USPATFULL on STN
        2003:37686
                      USPATFULL
AN
        Isolated homozygous stem cells, differentiated cells derived therefrom,
ΤI
        and materials and methods for making and using same Yan, Wen Liang, Potomac, MD, UNITED STATES Huang, Steve Chien-Wen, Germantown, MD, UNITED STATES Nguyen, Minh-Thanh, Rockville, MD, UNITED STATES
IN
        Lin, Hua, N. Potomac, MD, UNITED STATES
        Jingqi, Lei, Gaithersburg, MD, UNITED STATES
        Khanna, Ruchi, Germantown, MD, UNITED STATES
                                     20030206
        US 2003027331
                              Α1
PΙ
        US 2002-179959
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                                     20020626
                                               (10)
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        Continuation-in-part of Ser. No. US 2001-997240, filed on 30 Nov 2001,
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        US 2000-253943P
Utility
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PRAI
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 100 OF 313 USPA' 2003:23670 USPATFULL
L5
                           USPATFULL on STN
AN
        Encapsulated cell indicator system
TI
        Lee, Ike W., Norwood, MA, UNITED STATES
ΙN
        Ballica, Rabia, Framingham, MA, UNITED STATES
        Croissant, Jeffrey D., Scituate, MA, UNITED STATES
        US 2003017510
US 2002-121295
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 101 OF 313
                            USPATFULL on STN
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AN
        2003:17441 USPATFULL
ΤI
        Method of producing region-specific neurons from human neuronal stem
        cells
        Wu, Ping, League City, TX, UNITED STATES US 2003013193 A1 20030116
IN
PΙ
        US 2002-176971
US 2001-300344P
Utility
ΑĪ
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                                     20020619 (10)
PRĂI
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 102 OF 313
                            USPATFULL on STN
                      USPATFULL
AN
        2003:17440
TI
        Method for neural stem cell differentiation using valproate
        Laeng, Pascal, Washington, DC, UNITED STATES
IN
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Pitts, Lee, Falls Church, VA, UNITED STATES
        Psychiatric Genomics, Inc. (U.S. corporation)
PΑ
PI
                                      20030116
        US 2003013192
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        US 2002-175168
US 2001-299066P
Utility
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PRAI
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      ANSWER 103 OF 313
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AN
        2003:3443 USPATFULL
ΤI
        Identifying and characterizing genes
IN
        Depinho, Ronald A., Brookline, MA, UNITED STATES
        Chin, Lynda, Brookline, MA, UNITED STATES
                                      20030102
PI
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        US 2003003478
        US 2002-112503
US 2001-279506P
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        ICM: C12Q001-68
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CAS
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L_5
AN
        2003:3056 USPATFULL
        Directed in vitro differentiation of marrow stromal cells into neural
TI
        cell progenitors
        Prockop, Darwin J., New Orleans, LA, UNITED STATES Deng, Weiwen, Metairie, LA, UNITED STATES US 2003003090 Al 20030102
IN
PΙ
ΑI
        US 2002-153972
                                      20020523 (10)
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        US 2001-294281P
                                20010530 (60)
PRAI
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L5
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AN
        2003:332339
                       USPATFULL
TI
         cDNA libraries reflecting gene expression during growth and
        differentiation of human pluripotent stem cells
Funk, Walter D., Hayward, CA, United States
Carpenter, Melissa K., Foster City, CA, United States
IN
        Gold, Joseph D., San Francisco, CA, United States
Inokuma, Margaret S., San Jose, CA, United States
        Xu, Chunhui, Cupertino, CA, United States
        Geron Corporation, Menlo Park, CA, United States (U.S. corporation)
PA
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         INCLS: 435/366.000; 435/377.000; 435/320.100; 536/023.100

NCLM: 435/363.000

NCLS: 435/320.100; 435/366.000; 435/377.000; 536/023.100
NCL
IC
          [7]
         ICM: C12N005-06
         435/6; 435/320.1; 435/325; 435/455; 435/363; 435/366; 435/377; 536/23.1
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       ANSWER 106 OF 313
                               USPATFULL on STN
L5
AN
         2003:321559
                          USPATFULL
TI
         Modified protein derived from protein kinase N
         Kaibuchi, Kozo, Ikoma, JAPAN
Ono, Yoshitaka, Toyonaka, JAPAN
IN
         Iwamatsu, Akihiro, Yokohama, JAPAN
Kirin Beer Kabushiki Kaisha, Tokyo-To, JAPAN (non-U.S. corporation)
PA
                                          20031209
PI
         US 6660837
                                   B1
         US 1996-685852
                                          19960724 (8)
ΑI
         JP 1995-262552
PRAI
                                     19950914
         JP 1995-344606
                                     19951205
         JP 1996-80549
                                     19960308
         JP 1996-114226
                                     19960411
DT
         Utility
FS
         GRANTED
LN.CNT
         3868
INCL
         INCLM: 530/350.000
         INCLS: 530/300.000; 514/002.000; 514/012.000; 435/194.000; 435/320.100;
                   435/252.300; 435/252.330; 435/325.000; 536/023.100; 536/023.200;
                   536/023.500
                   530/350.000
435/194.000; 435/252.300; 435/252.330; 435/320.100; 435/325.000;
530/300.000; 536/023.100; 536/023.200; 536/023.500
         NCLM:
NCL
         NCLS:
IC
         ICM: C07K014-00
         ICS: C12N009-12
         435/194; 435/320.1; 435/252.3; 435/252.33; 435/325; 536/23.1; 536/23.2; 536/23.5; 530/300; 530/350; 514/2; 514/12
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 107 OF 313
2003:285185 USPA
                                USPATFULL on STN
ΑN
                          USPATFULL
TI
         Isolated mammalian neural stem cells, methods of making such cells
         Steindler, Dennis A., Memphis, TN, United States
Laywell, Eric D., Memphis, TN, United States
Kukekou, Valery G., Memphis, TN, United States
Thomas, L. Brannon, Johnson City, TN, United States
University of Tennessee Research Foundation, United States (U.S.
IN
PA
         corporation)
ΡI
         US 6638763
                                          20031028
         WO 9830678
                          19980716
         US 1999-402227
                                          19991001 (9)
AΙ
         WO 1998-US366
                                          19980107
PRAI
         US 1997-34910P
                                    19970107 (60)
         Utility
DT
FS
         GRANTED
LN.CNT
         974
         INCLM: 435/368.000
INCLS: 435/377.000; 435/384.000; 435/325.000
NCLM: 435/368.000
INCL
NCL
                   435/325.000; 435/377.000; 435/384.000
         NCLS:
IC
          [7]
         ICM: C12N005-08
         435/325; 435/377; 435/378; 435/379; 435/383; 435/384; 435/395; 435/402;
EXF
         435/368
L5
       ANSWER 108 OF 313
                                USPATFULL on STN
ΑN
         2003:129825
                          USPATFULL
{	t TI}
         Differentiation of human embryonic germ cells
         Gearhart, John D., Baltimore, MD, United States
Shamblott, Michael Joseph, Baltimore, MD, United States
The Johns Hopkins University School of Medicine, Baltimore, MD, United
IN
PA
         States (U.S. corporation)
PI
         US 6562619
                                   В1
                                          20030513
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Continuation of Ser. No. US 1998-52772, filed on 31 Mar 1998, now
RLI
        patented, Pat. No. US 6245566 Continuation-in-part of Ser. No. US 1997-989744, filed on 12 Dec 1997, now patented, Pat. No. US 6331406 Continuation-in-part of Ser. No. US 1997-829372, filed on 31 Mar 1997,
         now patented, Pat. No. US 6090622
         Utility
DT
FS
         GRANTED
LN.CNT
        1983
INCL
         INCLM: 435/366.000
         INCLS: 435/325.000; 424/093.210
                  435/366.000
NCL
         NCLM:
         NCLS:
                  424/093.210; 435/325.000
         [7]
IC
         ICM: C12N005-08
         435/325; 435/366; 435/440; 435/455; 800/8
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 109 OF 313 USPATFULL on STN
         2003:89280 USPATFULL
ΑN
TI
         Method of isolating ependymal neural stem cells
         Frisen, Jonas, Stockholm, SWEDEN
IN
         Janson, Ann Marie, Stockholm, SWEDEN
        Johansson, Clas, Stockholm, SWEDEN
Momma, Stefan, Sp.ang.nga, SWEDEN
Clarke, Diana, Stockholm, SWEDEN
        Zhao, Ming, Solna, SWEDEN
Lendahl, Urban, Sundbyberg, SWEDEN
Delfani, Kioumars, Solna, SWEDEN
Neuronova AB, Stockholm, SWEDEN (non-U.S. corporation)
PA
                                       20030401
PI
         US 6541247
                                 B1
         US 1998-104772
                                        19980625 (9)
AΙ
DT
         Utility
FS
         GRANTED
LN.CNT
         1146
INCL
         INCLM: 435/325.000
         INCLS: 435/007.100; 435/007.200; 435/007.210; 435/353.000; 435/354.000;
                  435/366.000; 435/368.000
                  435/325.000
NCL
         NCLM:
                  435/007.100; 435/007.200; 435/007.210; 435/353.000; 435/354.000;
         NCLS:
                  435/366.000; 435/368.000
IC
         [7]
         ICM: C12N005-00
         ICS: C12N005-02; C12N005-06; G01N033-53; G01N033-567 435/325; 435/352; 435/353; 435/354; 435/366; 435/368; 435/455; 435/7.1;
EXF
         435/7.2
      ANSWER 110 OF 313
                               CAPLUS COPYRIGHT 2004 ACS on STN
L_5
AN
      2004:637205
                      CAPLUS
TI
      Isolation and identification of retinal stem cells in mouse eye
      Wei, Yong; Ying, Dajun; Zhu, Chuhong; Zhang, Wei; Dong, Shiwu College of Basic Medicine, Third Military Medical University, Chongqing,
ΑU
CS
      400038, Peop. Rep. China
Di-San Junyi Daxue Xuebao (2003), 25(24), 2161-2164
SO
      CODEN: DYXUE8; ISSN: 1000-5404
PB
      Di-San Junyi Daxue Xuebao Bianjibu
DT
      Journal
      Chinese
LA
       ANSWER 111 OF 313 BIOENG COPYRIGHT on STN 2004 CSADUPLICATE 29
L5
                        BIOENG
AN
        2004449532
DN
        5614979
        Locally Born Olfactory Bulb Stem Cells Proliferate in Response to
TI
        Insulin-Related Factors and Require Endogenous Insulin-Like Growth
        Factor-I for Differentiation into Neurons and Glia
       Vicario-Abejon, C; Yusta-Boyo, MJ; Fernandez-Moreno, C; De Pablo, F
Group of Growth Factors in Vertebrate Development, Centro de
ΑU
CS
        Investigaciones Biologicas, Consejo Superior de Investigaciones
Cientificas, E-28006 Madrid, Spain
SO
        Journal of Neuroscience [J. Neurosci.]. Vol. 23, no. 3, pp. 895-906. Feb
        2003.
        ISSN: 0270-6474
DT
        Journal
LΑ
        English
SL
        English
OS
        CSA Neurosciences Abstracts; Chemoreception Abstracts
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ANSWER 112 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation.  $L_5$ STNAN2004:140379 BIOSIS PREV200400133731 DNEmbryonic Stage-Adult Sourced stem cells (ESAS) from bone marrow, and TI their neural differentiation in vitro. Qu, Xianlu [Reprint Author]; Jiang, Yajuan [Reprint Author]; Finklestein, ΑU Seth; Kraus, Morey; Visser, Jan [Reprint Author]; Perlingeiro, Rita [Reprint Author] Cambridge Research Center, ViaCell, Inc., Cambridge, MA, USA Blood, (November 16 2003) Vol. 102, No. 11, pp. 339a. print. Meeting Info.: 45th Annual Meeting of the American Society of Hematology. CS SO San Diego, CA, USA. December 06-09, 2003. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971. Conference; (Meeting) Conference; (Meeting Poster) DTConference; Abstract; (Meeting Abstract) LAEnglish Entered STN: 10 Mar 2004 ED Last Updated on STN: 10 Mar 2004 ANSWER 113 OF 313 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 30 L5 AN2004:395430 CAPLUS DN141:120783 Effects of GM1 on inducing adult rat bone marrow stromal cells to neural progenitor cells and their differentiation ΤI Zhang, Hui; Wang, Jizuo; Sun, Hongyu; Zhang, Wenzhi Department of Neurology, Tianjin Huanhu Hospital, Tianjin, 300060, Peop. CS Rep. China SO Zhonghua Shenjingke Zazhi (2003), 36(4), 283-286 CODEN: ZSZAFN; IŠSN: 1006-7876 PBZhonghua Yixuehui Zazhishe DTJournal LΑ Chinese ANSWER 114 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on L5STN AN2003:532692 BIOSIS PREV200300535744 DN TI Tales of transdifferentiation. Jin, Kunlin; Greenberg, David A. [Reprint Author] ΑU Buck Institute for Age Research, 8001 Redwood Boulevard, Novato, CA, CS 94945, USA dgreenberg@buckinstitute.org Experimental Neurology, (October 2003) Vol. 183, No. 2, pp. 255-257. SO print. CODEN: EXNEAC. ISSN: 0014-4886. DT Article English LA Entered STN: 12 Nov 2003 ED Last Updated on STN: 12 Nov 2003 ANSWER 115 OF 313 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 31 L5 2003:415190 ANCAPLUS DN 139:212169 TI Inhibition of endogenous VEGF impedes revascularization and astroglial proliferation: roles for VEGF in brain repair Krum, Janette M.; Khaibullina, Alfia AU Department of Anatomy and Cell Biology, George Washington University CS Medical Center, Washington, DC, 20037, USA Experimental Neurology (2003), 181(2), 241-257 CODEN: EXNEAC; ISSN: 0014-4886 SO PBElsevier Science DTJournal English LA ັ 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT ALL CITATIONS AVAILABLE IN THE RE FORMAT

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AN 2003:204797 BIOSIS

DN PREV200300204797

TI PACAP stimulates neuronal differentiation of cultured cortical precursor cells.

AU Arakawa, Naohisa [Reprint Author]; Iga, Junko [Reprint Author]; Shintani,

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Hitoshi [Reprint Author]; Baba, Akemichi [Reprint Author]
CS
      Lab. Mol. Neuropharmacol., Grad. Sch. Pharm. Sci., Osaka Univ., Suita,
      565-0871, Japan
      Journal of Pharmacological Sciences, (2003) Vol. 91, No. Supplement I, pp.
SO
      220P. print.
      Meeting Info.: 76th Annual Meeting of the Japanese Pharmacological
      Society. Fukuoka, Japan. March 24-26, 2003. Japanese Pharmacological
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      Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
DT
T.A
      English
ED
      Entered STN: 23 Apr 2003
      Last Updated on STN: 23 Apr 2003
      ANSWER 117 OF 313
L5
                                MEDLINE on STN
ΑN
      2003137180
                        MEDLINE
      PubMed ID: 12652649
***EGF*** -respo
DN
      ***EGF*** -responsive rat neural stem cells: molecular follow-up of neuron and astrocyte differentiation in vitro.
TI
      Jori F P; Galderisi U; Piegari E; Cipollaro M; Cascino A; Peluso G;
AU
      Cotrufo R; Giordano A; Melone M A B
      Department of Neurological Sciences, Second University of Naples, Naples,
CS
      Journal of cellular physiology, (2003 May) 195 (2) 220-33.
SO
      Journal code: 0050222. ISSN: 0021-9541.
CY
      United States
      Journal; Article; (JOURNAL ARTICLE)
DT
LΑ
      English
FS
      Priority Journals
EM
      200305
      Entered STN: 20030325
ED
      Last Updated on STN: 20030531
      Entered Medline: 20030530
                                     COPYRIGHT 2004 ACS on STN
L5
      ANSWER 118 OF 313 CAPLUS
      2003:973646
AN
                     CAPLUS
DN
      140:264804
      Effects of T3 on differentiation of human neural stem cells to
ΤI
      oligodendrocyte
      Liu, Ben; Li, Lanying; Liu, Chunrong; Pang, Zhiling
Institute of Endocrinology, Tianjin Medical University, Tianjin, 300070,
ΑU
CS
      Peop. Rep. China
      Jiepou Xuebao (2003), 34(2), 213-216
CODEN: CPHPA5; ISSN: 0529-1356
Jiepou Xuebao Bianji Weiyuanhui
SO
PB
DT
      Journal
      Chinese
LΑ
      ANSWER 119 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation.
L5
      STN
AN
      2004:168175
                     BIOSIS
DN
      PREV200400162081
TI
      Comparison of using serum free media vs. media with fetal bovine serum
      (FBS) in differentiation of mesenchymal stem cells (MSCs) into neural
      cells.
      Long, Xiaoxia [Reprint Author]; Olszewski, Marie L. [Reprint Author];
ΑU
      Huang, Wei [Reprint Author]; Kletzel, Morris [Reprint Author]
      Stem Cell Transplant Laboratory, Children's Memorial Hospital/Northwestern
CS
      University, Chicago, IL, USA
Blood, (November 16 2003) Vol. 102, No. 11, pp. 180b. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology.
San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
SO
      Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
DT
      English
LA
ED
      Entered STN: 24 Mar 2004
      Last Updated on STN: 24 Mar 2004
      ANSWER 120 OF 313 CAPLUS COPYRIGHT 2004 ACS on STN
L5
      2003:673295
AN
                     CAPLUS
DN
      139:302699
      Generation of cloned calves and transgenic chimeric embryos from bovine
TI
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embryonic stem-like cells

- Akira; Yamamoto, Yusuke; Hirayama, Hiroki; Kageyama, Soichi; Pan, Jianzhi; Murata, Takehide; Kobayashi, Yoshiro; Obata, Yuichi; Yokoyama, Kazunari K. Saito Laboratory of Cell Technology, Yaita, Tochigi, 329-1571, Japan CS
- SO Biochemical and Biophysical Research Communications (2003), 309(1), 104-113
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- PB Elsevier Science
- DT Journal English LA
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- ΤI Effect of cytokines on proliferation and differentiation of neural stem cells
- Zhang, Wenzhi; Su, Xin; Qin, Jinxi; Kong, Fanming; Kong, Jianguo; Wang, ΑU
- Xinping; Zhi, Dashi Department of Pathology, Tianjin Huanhu Hospital, Tianjin, 300060, Peop. CS Rep. China
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- PB Linchuang Yu Shiyan Binglixue Zazhi Bianjibu
- DT Journal
- LA Chinese
- ANSWER 122 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on L5 STN
- 2003:528897 BIOSIS AN
- PREV200300524702 DN
- TIISOLATION, CHARACTERIZATION AND EXPANSION OF PORCINE RETINAL PROGENITOR CELLS.
- Shatos, M. A. [Reprint Author]; Klassen, H.; Scherfig, E.; Kiilgaard, J. F.; Warfvinge, K.; Prause, J. U.; Young, M. J. [Reprint Author] Schepens Eye Research Institute, Boston, MA, USA ARVO Annual Meeting Abstract Search and Program Planner, (2003) Vol. 2003, ΑU
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- DT
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  Conference; (Meeting Poster) Conference; (Meeting Poster)
  Conference; Abstract; (Meeting Abstract)
- LΑ English
- Entered STN: 12 Nov 2003 ED
  - Last Updated on STN: 12 Nov 2003
- L5 ANSWER 123 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- 2004:205267 ANBIOSIS
- PREV200400205794 DN
- Conversion of human adult bone mesodermal stromal cells into neural stem TI cells.
- ΑU Hermann, A. [Reprint Author]; Gastl, R. [Reprint Author]; Fiedler, J.; Popa, O. M.; Liebau, S. [Reprint Author]; Schwarz, J.; Lerche, H.; Brenner, R.; Storch, A. [Reprint Author] Exptl. Neurol., Univ. Ulm, ULM, Germany
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  Conference; Abstract; (Meeting Abstract)
- DT
- LA English
- Entered STN: 14 Apr 2004 ED
  - Last Updated on STN: 14 Apr 2004
- L5BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. ANSWER 124 OF 313 on STN
- AN2004:146109 BIOSIS
- PREV200400145928 DN
- TITransduction of rat embryonic stem cells to overexpress neurotrophic factors using lentiviral vectors.
- ΑU Blits, B. [Reprint Author]; Gajavelli, S. [Reprint Author]; Tsoulfas, P.

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  - Last Updated on STN: 17 Mar 2004
- ANSWER 125 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. L5
- AN2004:146112 BIOSIS
- PREV200400145931 DN
- ΤI
- Long term culture of adult human and murine neural progenitor cells.
  Maisel, M. [Reprint Author]; Sabolek, M. [Reprint Author]; Hermann, A.
  [Reprint Author]; Liebau, S. [Reprint Author]; Antoniadis, G.; Sommer, C.;
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  Exptl. Neurol., Univ. of Ulm, Ulm, Germany
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  Vol. 2003, pp. Abstract No. 790 5 http://sfp.ccholarope.com of file ΑU
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- ED Entered STN: 17 Mar 2004
  - Last Updated on STN: 17 Mar 2004
- ANSWER 126 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on L5
- 2004:201242 BIOSIS AN
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- Meyer, M. [Reprint Author]; Andersen, R. K. [Reprint Author]; Johansen, M. [Reprint Author]; Blaabjerg, M. [Reprint Author]; Zimmer, J. [Reprint ΑU Author]
- Dept. Anat. and Neurobiol, SDU-Odense Univ, Odense C, Denmark CS
- Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) SO Vol. 2003, pp. Abstract No. 565.8. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience. Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
- DT
- LΑ English
- Entered STN: 14 Apr 2004 ED
  - Last Updated on STN: 14 Apr 2004
- ANSWER 127 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. L5STN
- AN2004:201220 BIOSIS
- DNPREV200400201778
- TI. Differentiation of radial qlia from embryonic stem cells in chemically defined medium.
- Liour, S. S. [Reprint Author]; Yu, R. K. AU
- Dept. of Neurol., Med. Col. of Georgia, Augusta, GA, USA CS
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  Conference; Abstract; (Meeting Abstract)
- DT
- LΑ English
- Entered STN: 14 Apr 2004 ED
  - Last Updated on STN: 14 Apr 2004
- ANSWER 128 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on L5STN
- AN2004:201202 BIOSIS
- DNPREV200400201760
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  Conference; Abstract; (Meeting Abstract)

DT

LAEnglish

- Entered STN: 14 Apr 2004 ED Last Updated on STN: 14 Apr 2004
- ANSWER 129 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. L5 STN
- 2004:199571 BIOSIS AN
- PREV200400200130 DNExpressions of chemokine receptors on neural stem cells from adult rat ΤI
  - [Reprint Author]; He, B. [Reprint Author]; Tay, S. S. W. [Reprint AU Ji, J. Authorl

CS

Anat., Natl. Univ. of Singapore, Singapore, Singapore Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) SO Vol. 2003, pp. Abstract No. 459.1. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience. Conference: (Meeting)

DT Conference; Abstract; (Meeting Abstract)

English LA

EDEntered STN: 14 Apr 2004 Last Updated on STN: 14 Apr 2004

ANSWER 130 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. L5 STN

2004:199504 BIOSIS AN

PREV200400200063 DNΤI

ΑU

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DT

LА English

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- ANSWER 131 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. L5
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DN PREV200400200024

- Human retinal progenitor cells can be cultured from postmortem tissue and express a range of known primitive and mature markers. TI
- ΑU
- Klassen, H. [Reprint Author]; Schwartz, P. H. [Reprint Author]; Ziaeian, B. [Reprint Author]; Kirov, I. I. [Reprint Author]; Young, M. J. Stem Cell. Res., Children's Hosp. of Orange County, Orange, CA, USA Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) CS SO Vol. 2003, pp. Abstract No. 453.3. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience. Conference; (Meeting)
  Conference; Abstract; (Meeting Abstract)

DT

English LΑ

- Entered STN: 14 Apr 2004 ED Last Updated on STN: 14 Apr 2004
- ANSWER 132 OF 313 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. L5
- 2004:199466 BIOSIS AN
- DNPREV200400200025
- TI
- Banking human neural stem cells from postmortem brain. Schwartz, P. H. [Reprint Author]; Ziaeian, B. [Reprint Author]; Kirov, I. [Reprint Author]; Fuja, T.; Su, H.; Bryant, P. J.; O'Dowd, D. K.; AU

Children's Hosp. of Orange County, Univ. of California, Irvine, CA, USA Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) CS SO Vol. 2003, pp. Abstract No. 453.4. http://sfn.scholarone.com. e-file. Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience. Conference; (Meeting) DT Conference; Abstract; (Meeting Abstract) LA English EDEntered STN: 14 Apr 2004 Last Updated on STN: 14 Apr 2004 TOXCENTER COPYRIGHT 2004 ACS on STN ANSWER 133 OF 313 L5 2004:19730 TOXCENTER AN DART-TER-3001508 DN Analysis of mouse cytomegalovirus susceptibility in brain slices. TI Kawasaki H; Kosugi İ; Baba S; Tsuchida T; Li R Y; Arai Y; Furuta K; ΑU Ishiwata M; Tsutsui Y 2nd Department of Pathology, Hamamatsu University School of Medicine, CS Shizuoka, Japan. Congenit Anom Kyoto, (2002 Sep) 42 (3) 246. SO ISSN: 0914-3505 Abstract; (MEETING ABSTRACT) DTFS DART English LA Entered STN: 20040203 EDLast Updated on STN: 20040203 TOXCENTER COPYRIGHT 2004 ACS on STN ANSWER 134 OF 313 L5 TOXCENTER 2004:19687 ANDART-TER-3001465 DNMechanisms of developing brain disorders induced by cytomegalovirus. ΤI ΑU Second Department of Pathology, Hamamatsu University School of Medicine, CS Hamamatsu, Shizuoka, Japan. Congenit Anom Kyoto, (2002 Sep) 42 (3) 228-30. SO ISSN: 0914-3505 Abstract; (MEETING ABSTRACT) DT FS DART LA English Entered STN: 20040203 ED Last Updated on STN: 20040203 ANSWER 135 OF 313 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN L5 DUPLICATE 32 2002-14142 BIOTECHDS ANCellular composition useful for transplantation purposes, comprises a TI population of multipotent mammalian cells that are self-renewing, and capable of forming non-adherent clusters in culture; genetically modified stem cell differentiation and epithelium tissue culture for disease therapy and tissue engineering TOMA J; AKHAVAN M; FERNANDES K J L; FORTIER M; MILLER F TOMA J; AKHAVAN M; FERNANDES K J L; FORTIER M; MILLER F ΑU PA US 2002016002 7 Feb 2002 US 2000-916639 24 Jan 2000 PΙ ΑI US 2001-916639 26 Jul 2001 PRAI DTPatent English LAWPĬ: 2002-239226 [29] OS CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 33 ANSWER 136 OF 313  $L_5$ 2002:674692 CAPLUS ANDN 137:181930 Multipotent stem cells from peripheral tissues and uses thereof TI Toma, Jean; Akhavan, Mahnaz; Fernandes, Karl J. L.; Fortier, Mathieu; IN Miller, Freda PA U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 916,639. SO CODEN: USXXCO DT Patent English LAFAN.CNT 7 DATE APPLICATION NO. KIND DATE PATENT NO. 20011109 US 2001-991480 PΙ US 2002123143 A120020905 US 2000-670049 20000925 US 6787355 20040907 B1

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         EMBRYONIC STEM CELLS AND NEURAL PROGENITOR CELLS DERIVED THEREFROM;
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         REGENERATION CELLS OF NERVOUS SYSTEM
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           38 Figure(s).
        FIG. 1 shows phase contrast micrographs of ES cells and their
        differentiated progeny. A, inner cell mass three days after plating. B, colony of ES cells. C, higher magnification of an area of an ES cell colony. D, an area of an ES cell colony undergoing spontaneous differentiation during routine passage. E, a colony four days after plating in the absence of a feeder cell layer but in the presence of 2000 units/ml human LIF undergoing differentiation in its periphery,. F, neuronal cells in a high density culture. Scale bars: A and C, 25 microns; B and E, 100 microns; D and F, 50 microns.

FIG. 2 shows marker expression in ES cells and their differentiated somatic progeny. A. ES cell colony showing histochemical staining for
          somatic progeny. A, ES cell colony showing histochemical staining for
          alkaline phosphatase. B. ES cell colony stained with antibody MC-813-70
         recognising the SSEA-4 epitope. C, ES cell colony stained with antibody TRAL-60. D, ES cell colony stained with antibody GCTM-2. E, high density culture, cell body and processes of a cell stained with antineurofilament 68 kDa protein. F, high density culture, cluster of cells and network of processes emanating from them stained with antibody against neural cell adhesion molecula. C high density culture, cells showing cutonics.
          adhesion molecule. G, high density culture, cells showing cytoplasmic
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cell showing cytoplasmic filaments stained with antibody to desmin. Scale bars: A, 100 microns; B-D, and F, 200 microns; E, G and H, 50 microns.
FIG. 3 shows RT-PCR analysis of gene expression in ES cells and their differentiated derivatives. All panels show 1.5% agarose gels stained
  with ethidium bromide. A, expression of Oct-4 and b-actin in ES stem cells and high density cultures. Lane 1, 100 bpDNA ladder. Lane 2, stem cell culture, b-actin. Lane 3, stem cell culture, Oct-4. Lane 4, stem cell culture, PCR for Oct-4 carried out with omission of reverse transcripts as a lane 5 bigh density culture.
transcriptase. Lane 5, high density culture, b-actin. Lane 6, high density culture, Oct-4. Lane 7, high density culture, PCR for Oct-4 carried out with omission of reverse transcriptase. b-actin band is 200
                                                                                                                       ***nestin***
                                                                                                                                                             and Pax-6
  bp and Oct-4 band is 320 bp. B, expression of
  in neural progenitor cells that were derived from differentiating ES colonies. Left lane, 100 bp DNA ladder; lane 1, b-actin in HX 142 neuroblastoma cell line (positive control for ***nestin*** PCR)
                                                                                                                                     ***nestin***
  lane 2, b-actin in neural progenitor cells; lane 3, ***nestin***
HX 142 neuroblastoma cell line; lane 4, ***nestin*** in neural progenitor cells; lane 5, ***nestin*** PCR on same sample as 1
                                                                                                           PCR on same sample as lane 4
  progenitor cells; lane 5,
  without addition of reverse transcriptase; lane 6, Pax-6; lane 7, Pax-6 PCR on same sample as line 6 without addition of reverse transcriptase.
  ***Nestin*** band is 208 bp, Pax-6 is 274 bp. C, expression of glutam: acid decarboxylase in cultures of neurons. Left lane, 100 bp DNA ladder;
   lane 1, b-actin; lane 2, b-actin PCR on same sample as lane 1 without
  addition of reverse transcriptase; lane 3, glutamic acid decarboxylase; lane 4 glutamic acid decarboxylase on same sample as lane 3 without addition of reverse transcriptase. Glutamic acid decarboxylase band is 284 bp. D, expression of GABA A alpha 2 receptor. Left lane, 100 bp DNA ladder; lane 1, b-actin; lane 2, GABA A alpha 2 receptor; lane 3, PCR without addition of reverse transcriptage. GABA A alpha 2 receptor.
   without addition of reverse transcriptase. GABA A alpha 2 receptor subunit band is 471 bp.
FIG. 4 shows histology of differentiated elements found in teratomas
   formed in the testis of SCID mice following inoculation of HES-1 or HES-2 colonies. A, cartilage and squamous epithelium, HES-2. B, neural
colonies. A, cartilage and squamous epithelium, HES-2. B, neural rosettes, HES-2. C, ganglion, gland and striated muscle, HES-1. D, bone and cartilage, HES-1. E, glandular epithelium, HES-1. F, ciliated columnar epithelium, HES-1. Scale bars: A-E, 100 microns; F, 50 microns. FIG. 5 shows phase contrast microscopy and immunochemical analysis of marker expression in neural progenitor cells isolated from differentiating ES cultures. A, phase contrast image of a sphere formed in serum-free medium. B-D, indirect immunofluorescence staining of spheres. A hours after plating on adhesive substrate. For N-CAM
  spheres, 4 hours after plating on adhesive substrate, for N-CAM,
***nestin***, and vimentin respectively. In C and D, cells at the base
of the sphere were placed in plane of focus to illustrate filamentous
staining; confocal examination revealed that cells throughout the sphere
were decorated by both antibodies. Scale bar is 100 microns in all
   panels.
 FIG. 6 shows phase contrast appearance and marker expression in cultures
   of neurons derived from progenitor cells shown in FIG. 5. A, phase
   contrast micrograph of differentiated cells emanating from a sphere
   plated onto adhesive surface. B-H, indirect immunofluorescence microscopy
of differentiated cells decorated with antibodies against 200 kDa neruofilament protein (B), 160 kDa neurofilament protein (C), MAP2a+b (D), glutamate (E), synaptophysin (F), glutamic acid decarboxylase (G) and beta-tubulin (H). Scale bars: A, ;B, 100 microns; C, 200mircons; D, 20 microns; E and F, 10 microns; G, 20 microns; H, 25 microns. FIG. 7 shows neural precursors proliferating as a monolayer on a plastic tissue culture dish in the presence of ***EGF*** and ***bFGF***
   tissue culture dish in the presence of ***EGF*** and ***bFGF*
These monolayer cultures of proliferating cells were obtained after
   prolonged cultivation (2-3 weeks) of the spheres in the presence of
   growth factors without sub-culturing.
 FIG. 8 shows phase contrast appearance of a culture consisting of
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differentiated neural cells.

FIG. 9 shows phase contrast appearance of a sphere that is formed 72 hours after the transfer of a clump of undifferentiated ES cells into serum free medium (Scale bar 100 microns).

FIG. 10 shows linear correlation between the volume of spheres and the

number of progenitor cells within a sphere. Spheres of various diameters that were generated from differentiating ES colonies and were propagated for 14-15 weeks were dissaggregated into single cell suspension and the number of cells per sphere was counted.

FIG. 11 shows indirect immunofluorescence staining of a sphere, 4 hours after plating on adhesive substrate, for N-CAM. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of the resulting spheres for 5 passages. (Scale bar 100 migrans) microns).

of single cells at the periphery of a sphere 4 hours after plating on adhesive substrate. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of the resulting spheres for 5 passages. (Scale bar 25 microns). FIG. 13 shows indirect immunofluorescence staining of a spheres 4 hours after plating on adhesive substrate for the intermediate filament \*\*\*nestin\*\*\* . Cells at the base of the sphere were placed in . Cells at the base of the sphere were placed in plane of focus to illustrate filamentous staining. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of resulting spheres for 5 passages. (Scale bar 25 microns). FIG. 14 shows indirect immunofluorescence microscopy of a differentiated cell decorated with antibodies against the oligodendrocyte progenitor marker 04. (Scale bar 12.5 microns). FIG. 15 shows indirect immunofluorescence staining of a sphere 4 hours after plating on adhesive substrate for the intermediate filament vimentin. Cells at the base of the sphere were placed in plane of focus to illustrate filamentous staining. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of resulting spheres for 7 passages. (Scale bar 25 microns). FIG. 16 shows the growth pattern of spheres that were generated directly from undifferentiated ES cells. Each bar represents the mean (+-SD) increment in volume per week of 24 spheres at first to sixteen weeks after derivation. A more excessive growth rate is evident during the first 5 weeks. FIG. 17 shows persistent growth in the volume of spheres along time. Each bar represents the mean (+-SD) increment in volume per week of 24 spheres at nine to twenty one weeks after derivation. The spheres were generated from differentiating ES colonies. FIG. 18 shows linear correlation between the volume of spheres and the number of progenitor cells within a sphere. Spheres of various diameters, that were generated directly from undifferentiated ES cells and were propagated 5-7 weeks, were dissaggregated into single cell suspension and the number of cells per sphere was counted.
FIG. 19 shows RT-PCR analysis of gene expression in ES cells (a week after passage) and neural spheres derived from differentiating colonies and directly from undifferentiated ES cell. All panels show 2% agarose gels stained with ethidium bromide. Lanes 1, 2 and 3, Oct-4 in ES cell culture, neural spheres derived from differentiating colonies, neural spheres derived from undifferentiated ES cells. Lane 4, stem cell culture, PCR for Oct-4 carried out with omission of reverse transcriptase. Lanes 5, 6, and 7, \*\*\*nestin\*\*\* in ES cell culture, neural spheres derived from differentiating colonies, neural spheres derived from undifferentiated ES cells. Lane 8, stem cell culture, PCR for \*\*\*nestin\*\*\* carried out with omission of reverse transcriptase \*\*\*nestin\*\*\* carried out with omission of reverse transcriptase. Lanes 9, 10 and 11, Pax-6 in ES cell culture, neural spheres derived from differentiating colonies, neural spheres derived from undifferentiated ES cells. Lane 12, stem cell culture, PCR for Pax-6 carried out with omission of reverse transcriptase. Lane 13, 100 bp DNA ladder. Oct-4 band is 320 bp, \*\*\*nestin\*\*\* is 208 bp and Pax-6 is 274 bp. FIG. 20 shows indirect immunofluorescence microscopy of differentiated astrocyte cells decorated with antibody against \*\*\*GFAP\*\*\* . (Scale astrocyte cells decorated with antibody against bar 25 microns) FIG. 21 shows indirect immunofluorescence microscopy of brain sections of two mice (A and B) 4 weeks after transplantation of human neural precursors prelabeled with BrDU. Cells with a nucleus decorated with anti BrDU (brown stain, black arrow) are evident near the ventricular surface (white arrow indicate mouse unstained nuclei, bar=20 microns).

FIG. 22 shows indirect immunofluorescence microscopy of brain sections of a mice 4 weeks after transplantation of human neural precursors prelabeled with BrDU Wide spread distribution of transplanted human prelabeled with BrDU. Wide spread distribution of transplanted human cells decorated by anti BrDU antibodies is evident in the periventricular areas. The periventricular area in A is demonstrated at a higher magnification in B and C. (Bars=150, 60 and 30 microns in A, B and C).

FIG. 23 shows indirect immunocytochemical microscopy of brain sections of a mice 4 weeks after transplantation of human neural precursors prelabeled with BrDU. The transplanted human cells are migrating along the rostral migratory stream (bar=150 microns).

FIG. 24 shows RT-PCR analysis of gene expression in neural spheres derived from differentiating (A) and undifferentiated (B) ES cells. All panels show 2% agarose gels stained with ethidium bromide. Lanes 1 and 10, 100 bpDNA ladder: Lane 2. CD34: Lane 3. Flk-1: lane4, HNF-3: lane 5, bpDNA ladder; Lane 2, CD34; Lane 3, Flk-1; lane4, HNF-3; lane 5, alfafetoprotein. Lanes 6-9 PCR reaction on the same samples as lanes 2-5 carried out with the omission of reverse transcriptase. CD-34 band is 200 bp, Flk-1 is 199, HNF-3 is 390, AFP is 340 bp. FIG. 25 shows by RT-PCR analysis the expression of \*\*\*GFAP\*\*\*

differentiating ES cell colonies. The expression of \*\*\*GFAP\*\*\* indicates differentiation into astrocytes while the presence of both dm-20 and pip transcripts indicate that differentiation into oligodendrocyte cells has occurred. Lanes 2, 4, 6 and lanes 3, 5, 7 are from two separate RNA samples from differentiated spheres that were independently derived from ES cells. Lane 1 and 8, 100 bp DNA ladder; Lanes 2 and 4, \*\*\*GFAP\*\*\*; lanes 3 and 5, plp and dm-20; lanes 6 and 7, PCR reaction on the same samples as lanes 3 and 5 carried out with the omission of reverse transcriptase. \*\*\*GFAP\*\*\* band is 383, pip band omission of reverse transcriptase. \*\*\*GFAP\*\*\* band is 383, pip band is 354 bp and dm-20 is 249 bp.

FIG. 26 shows a dark field stereomicroscopic photograph of areas (arrows) destined to give rise to neural precursors in a differentiating ES cell colony 3 weeks after passage (bar=1.6 mm).

FIG. 27 shows indirect immunochemical analysis of marker expression in gultures of neurons derived from progenitor cells that were derived

cultures of neurons derived from progenitor cells that were derived directly from undifferentiated ES cells: A, indirect immunofluorescence microscopy of neurits decorated with antibody against 160 kDa neurofilament protein. B and C, indirect immunofluorescence staining of differentiated cells for MAP2a+b and beta-tubulin III. Scale bars: A 100 microns, B and C 10 microns.

FIG. 28 shows indirect immunochemical analysis of the expression of tyrosine hydroxylase. Neurits (A) and a differentiated cell (B) are decorated with antibodies against tyrosine hydroxylase. Scale bars: 30

microns.

FIG. 29 shows in vivo differentiation into astrocyte cells of transplanted human neural progenitors prelabeled with BrDU. Donor cells are identified by indirect immunochemical detection of BrDU (dark nuclei, arrows). Duel staining demonstrates donor cells decorated by anti \*\*\*GFAP\*\*\* staining demonstrates donor cells decorated by anti-(orange). Transplanted cells are migrating into the brain parenchyma (white arrow) and are also found in the periventricular zone (dark arrow) (A), A higher magnification of cells that have differentiated into astrocytes and migrated into the host brain (B).

FIG. 30 shows in vivo differentiation into oligodendrocyte cells of transplanted human neural progenitors prelabeled with BrDU. Donor cells are identified by indirect immunochemical detection of BrDU (dark nuclei, arrows). Duel staining demonstrates donor cells decorated by anti CNPase

(orange).

FIG. 31 shows cumulative growth curve for human neural progenitors derived from differentiating colonies. (A) Continuous growth is evident during an 18-22 week period. The increment in the volume of the spheres was continuously monitored as an indirect measure of the increase in cell numbers. A linear positive correlation between the volume of the spheres and the number of cells within the spheres (B, insert) was maintained

and the number of cells within the spheres (b, insert) was maintained along cultivation. It supported the validity of monitoring the increment of sphere volume as an indirect indicator of cell proliferation.

FIG. 32 shows RT-PCR analysis of the expression of non-neural markers in human ES derived spheres. All panels show 2% agarose gels stained with ethidium bromide. The symbols + and indicate whether the PCR reaction was performed with or without the addition of reverse transcriptase. A 1 Kb plus DNA ladder was used in all panels. beta-actin band is 291 bp, keratin is 780 bp, Flk-1 is 199 bp, CD34 is 200 bp, AC-133 is 200 bp, transferin is 367 bp, amylase is 490 bp and alpha 1 anti trypsin is 360

FIG. 33 shows a phase contrast micrograph of differentiated cells growing out from a sphere 2 weeks after plating onto an adhesive surface and culture in the absence of growth factors. Scale bar is 200 mu m. FIG. 34 shows RT-PCR analysis of the expression of neuronal and glial

markers in differentiated cells originating from human ES derived neural spheres. All panels show 2% agarose gels stained with ethidium bromide. The symbols + and -indicate whether the PCR reaction was performed with or without the addition of reverse transcriptase. A 1 Kb plus DNA ladder was used in all panels. Plp and dm-20 bands are 354 bp and 249 bp respectively, MBP is 379 bp, \*\*\*GFAP\*\*\* is 383 bp, NSE is 254 bp and respectively, MBP is 379 bp, NF-M is 430 bp.

FIG. 35 shows indirect immunochemical analysis of the expression of

serotonin (A) and GABA (B). Scale bars are 20 mu m. FIG. 36 shows dissemination of transplanted BrdU+ human ESderived neural progenitor cells in the mouse host brain.

(A) At 2 days after transplantation most cells were found lining the ventricular wall. (B) After 4-6 weeks most cells had left the ventricles (V) and populated the corpus callosum (CC), fimbria (fim), internal capsule (i.c.). BrdU+ cells were not found in the striatum (str) or CA region of the hippocampus (hipp). (C) Chains of BrdU+ cells were found in the rostral migratory stream (RMS). (D) BrdU+ cells in the periventricular white matter. (E) Higher magnification of D, to show FIG. 37 shows identification of the transplanted cells in the brain by human and neural-lineage specific markers. (A) A typical chain of transplanted cells in the brain by transplanted cells in the corpus callosum, stained with human specific anti-mitochondrial antibody. The mitochondrial staining (green fluorescence) on Nomarsky background (blue, cell nuclei indicated by asterisk) shows a typical perinuclear localization. (B) Double staining for BrdU (green fluorescence) and human specific anti ribonuclear protein (red fluorescence) shows nuclear co-localization, indicating that BrdU+ cells were indeed of human origin. (C) A \*\*\*GFAP\*\*\* + astrocyte (red) from the periventricular region, colabeled with BrdU (green), indicating its origin from the graft. (D) An NG2+ oligodendrocyte progenitor (red) in the periventricular region, co-labeled with BrdU (green). (E) A CNPase+ oligodendrocyte (red) in the corpus callosum, colabeled with BrdU (immunohistochemistry, shown as dark nucleus in Nomarsky). (F) Neuronal processes in the fimbria, stained with a human specific anti-70 kDa neurofilament. (G) A beta III-tubulin+ neuron (green fluorescence) in the olfactory bulb, co-labeled with BrdU (as dark nucleus (arrow) in Nomarsky). Bars=10 mu m. !

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BONE MARROW CELLS AS A SOURCE OF NEURONS FOR BRAIN AND SPINAL CORD TIREPAIR; BONE-MARROW DERIVED NEURONAL CELLS FOR USE IN THE TREATMENT OF NERVOUS SYSTEM DISORDERS

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DT Utility; Patent Application - First Publication

FS CHEMICAL APPLICATION

CLMN 20

8 Figure(s). GI

FIG. 1 is a bar graph. BMSC adherent to culture dishes were treated with \*\*\*EGF\*\*\* (10 ng/ml), RA (0.5 mu M) or RA plus BDNF (10 ng/ml) for 7 days. Each bar represents the mean number (+-SEM) of fibronectin immunoreactive cells per visual field 20 x objective) determined in 20 fields per dish in 4 culture dishes. \*=p less-than 0.05, two-tailed t-test FIGS. 2A through 2F are photomicrographs of BMSC from lacz mice that have been cocultured with mouse fetal midbrain cells for 2 weeks in N5 medium supplemented with cis-9 retinoic acid (0.5 mu M) and BDNF (10

FIGS. 3A through 3F are photomicrographs, which illustrate the migration and integration of BMSC into rat midbrain. FIG. 3A (scale bar=500 mu m) shows symmetrical distribution despite unilateral grafting into the striatum. FIG. 3B is a region of the paraventricular nucleus (scale bar=100 mu m). None of the beta-gal+ cells are labeled with the red-brown stain (TH-ir). FIGS. 3A (Scale bar=500 mu m), 3B (Scale bar=100 mu m) and 3C (Scale bar=50 mu m) depict cells doubly stained for beta-gal and TH-ir. FIGS. 3D (Scale bar=50 mu m) and 3E (Scale bar=25 mu m) illustrate sections from the red nucleus that have doubly stained for beta-gal and NewN-ir FIG. 3E (Scale bar=25 mu m) illustrates beta-gal+ cells from the NeuN-ir. FIG. 3F (Scale bar=25 mu m) illustrates beta-gal+ cells from the red nucleus also doubly stained for MAP2-ir.

FIGS. 4A through 4F are photomicrographs of a section from rat cerebellar lobule illustrating laminar distribution of betagal+ cells in a distribution of Purkinje cells. alpha-gal+ are co-labeled with calbindin immunoreactivity in FIGS. 4A, 4B, and 4C. (Scale bar=100 mu m in 4A, 50 mu m in 4B and 25 mu m in 4C). FIG. 4D shows beta-gal+ Purkinje cells co-labeled with GAD-ir (Scale bar=50 mu m). FIG. 4E illustrates dense MAP2-ir fibers everloping beta-gal+ Purkinje cells (Scale bar=25 mu m). FIG. 4F illustrates beta-gal+ cells co-labeled with NeuN-ir in the deep cerebellar nucleus (Scale bar=25 mu m).

FIGS. 5A through 5D are photomicrographics showing the production of markers for fibronectin (FIG. 5A) and differentiated BMSC with nerve cell

markers (FIGS. 5B, 5C and 5D). FIG. 6 is a Western blot of the lysates of BMSC conditioned with four different treatments and labeled with \*\*\*GFAP\*\*\* -ir, \*\*\*nestion and NeuN. BDNF+RA+N5 induced the strongest expression of nerve cell

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FIGS. 7A through 7F are photomicrographs of human BMSC which were co-cultured with fetal rat striatal cells in N5 formulation with BDNF+RA. These figures show that human BMSC (green labeled in FIGS. 7C and 7D and yellow in FIGS. 7E and 7F) can be induced to express neural markers NeuN (FIGS. 7A and 7E) and ***GFAP*** (FIGS. 7B and 7F).
FIG. 8 is a photomicrograph of rat brain, showing that mouse BMSC labeled
  with red PKH26 also express the neuron marker NeuNir (green fluorescence). In addition, the morphology of the doubly labeled cells is
   that of neurons.
FIG. 9 is a photomicrograph of rat brain, showing a doubly labelled glial
   cell. The red fluorescent tracer identifies it as derived from a BMSC,
                                                                                                   ***GFAP***
  and the green fluorescence is due to
                                                                                                                                -ir. Note the
  morphology is that of a glial cell.
                                               IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 36
ANSWER 139 OF 313
                            IFIPAT; IFIUDB; IFICDB
  EMBRYONIC STEM CELLS AND NEURAL PROGENITOR CELLS DERIVED THEREFROM; SUCH
  AS NEURAL PROGENITOR CELLS CAPABLE OF GIVING RISE TO MATURE SOMATIC CELLS
   INCLUDING NEURAL CELLS AND/OR GLIAL CELLS RECOGNIZABLE BY EXPRESSION OF
   SPECIFIC MARKERS
  Ben-Hur Tamir (IL); Pera Martin Frederick (AU); Reubinoff Benjamin Eithan
   (IL)
  Unassigned Or Assigned To Individual (68000)
                                                     20020606
          2002068045
                                         A1
  US 2001-808382
                                                     20010314
  AU 2000-6211
                                                     20000314
  AU 2000-1279
                                                     20001106
  AU 2001-2920
                                                     20010206
  US 2002068045
                                                     20020606
  Utility; Patent Application - First Publication
   CHEMICĀL
  APPLICATION
     30 Figure(s).
FIG. 1 shows phase contrast micrographs of ES cells and their
differentiated progeny. A, inner cell mass three days after plating. B, colony of ES cells. C, higher magnification of an area of an ES cell colony. D, an area of an ES cell colony undergoing spontaneous differentiation during routine passage. E, a colony four days after plating in the absence of a feeder cell layer but in the presence of 2000 units/ml human LIF undergoing differentiation in its periphery, F, neuronal cells in a high density culture. Scale bars: A and C, 25 microns; B and E, 100 microns; D and F, 50 microns.

FIG. 2 shows marker expression in ES cells and their differentiated somatic progeny. A, ES cell colony showing histochemical staining for
  somatic progeny. A, ES cell colony showing histochemical staining for alkaline phosphatase. B. ES cell colony stained with antibody MC-813-70
  recognising the SSEA-4 epitope. C, ES cell colony stained with antibody TRA1-60. D, ES cell colony stained with antibody culture, cell body and processes of a cell stained with antineurofilament 68 kDa protein. F, high density culture, cluster of cells and network of processes emanating from them stained with antibody against neural cell adhesion molecule. G, high density culture, cells showing cytoplasmic filaments stained with antibody to muscle actin. H, high density culture, cell showing cytoplasmic filaments stained with antibody to desmin. Scale bars: A, 100 microns: B-D, and F, 200 microns: E, G, and H, 50 microns
bars: A, 100 microns; B-D, and F, 200 microns; E, G and H, 50 microns. FIG. 3 shows RT-PCR analysis of gene expression in ES cells and their differentiated derivatives. All panels show 1.5% agarose gels stained with ethidium bromide. A, expression of Oct-4 and-b-actin in ES stem cells and high density cultures. Lane 1, 100 bpDNA ladder. Lane 2, stem cell culture, b-actin. Lane 3, stem cell culture, Oct-4. Lane 4, stem cell culture, PCR for Oct-4 carried out with omission of reverse transcriptase. Lane 5, high density culture, b-actin. Lane 6, high density culture. PCR for Oct-4
  density culture, Oct-4. Lane 7, high density culture, PCR for Oct-4 carried out with omission of reverse transcriptase. b-actin band is 200
  bp and Oct-4 band is 320 bp. B, expression of ***nestin*** and Pain neural progenitor cells that were derived from differentiating ES colonies. Left lane, 100 bp DNA ladder; lane 1, b-actin in HX 142 neuroblastoma cell line (positive control for ***nestin*** PCR) lane 2, b-actin in neural progenitor cells; lane 3, ***nestin*** HX 142 neuroblastoma cell line; lane 4, ***nestin*** in neural progenitor cells; lane 5, ***nestin*** PCR on same sample as lane
  progenitor cells; lane 5, ***nestin*** PCR on same sample as lane 4 without addition of reverse transcriptase; lane 6, Pax-6; lane 7, Pax-6 PCR on same sample as line 6 without addition of reverse transcriptase.
        ***Nestin***
                                          band is 208 bp, Pax-6 is 274 bp. C, expression of glutam:
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lane 1, b-actin; lane 2, b-actin PCR on same sample as lane 1 without addition of reverse transcriptase; lane 3, glutamic acid decarboxylase; lane 4 glutamic acid decarboxylase on same sample as lane 3 without addition of reverse transcriptase. Glutamic acid decarboxylase band is 284 bp. D, expression of GABA A alpha 2 receptor. Left lane, 100 bp DNA ladder; lane 1, b-actin; lane 2, GABA A alpha 2 receptor; lane 3, PCR without addition of reverse transcriptase. GABA A alpha 2 receptor subunit band is 471 bp.

FIG. 4 shows histology of differentiated elements found in teratomas formed in the testis of SCID mice following inoculation of HES-1 or HES-2 colonies. A, cartilage and squamous epithelium, HES-2. B, neural rosettes, HES-2. C, ganglion, gland and striated muscle, HES-1. D, bone and cartilage, HES-1. E, glandular epithelium, HES-1. F, ciliated columnar epithelium, HES-1. Scale bars: A-E, 100 microns; F, 50 microns. FIG. 5 shows phase contrast microscopy and immunochemical analysis of

marker expression in neural progenitor cells isolated from differentiating ES cultures. A, phase contrast image of a sphere formed in serum-free medium. B-D, indirect immunofluorescence staining of spheres, 4 hours after plating on adhesive substrate, for N-CAM,

\*\*\*nestin\*\*\*, and vimentin respectively. In C and D, cells at the base of the sphere were placed in plane of focus to illustrate filamentous staining; confocal examination revealed that cells throughout the sphere were decorated by both antibodies. Scale bar is 100 microns in all

FIG. 6 shows phase contrast appearance and marker expression in cultures of neurons derived from progenitor cells shown in FIG. 5. A, phase contrast micrograph of differentiated cells emanating from a sphere plated onto adhesive surface. B-H, indirect immunofluorescence microscopy of differentiated cells decorated with antibodies against 200 kDa neurofilament protein (B), 160 kDa neurofilament protein (C), MAP2a+b

(D), glutamate (E), synaptophysin (F), glutamic acid decarboxylase (G) and beta-tubulin (H). Scale bars: A,;B, 100 microns; C, 200 mircons; D, 20 microns; E and F, 10 microns; G, 20 microns; H, 25 microns.

FIG. 7 shows neural precursors proliferating as a monolayer on a plastic tissue culture dish in the presence of \*\*\*EGF\*\*\* and \*\*\*bFGF\*\*\*

These monolayer cultures of proliferating cells were obtained after prolonged cultivation (2-3 weeks) of the spheres in the presence of

growth factors without sub-culturing.

FIG. 8 shows phase contrast appearance of a culture consisting of differentiated neural cells.

FIG. 9 shows phase contrast appearance of a sphere that is formed 72 hours

after the transfer of a clump of undifferentiated ES cells into serum free medium (Scale bar 100 microns).

FIG. 10 shows linear correlation between the volume of spheres and the number of progenitor cells within a sphere. Spheres of various diameters that were generated from differentiating ES colonies and were propagated for 14.15 works were diagrammented into a sphere. for 14-15 weeks were dissaggregated into single cell suspension and the number of cells per sphere was counted.

FIG. 11 shows indirect immunofluorescence staining of a sphere, 4 hours after plating on adhesive substrate, for N-CAM. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of the resulting spheres for 5 passages. (Scale bar 100

microns)

FIG. 12 shows indirect immunofluorescence membraneous staining for N-CAM of single cells at the periphery of a sphere 4 hours after plating on adhesive substrate. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of the resulting spheres for 5 passages. (Scale bar 25 microns).

FIG. 13 shows indirect immunofluorescence staining of a spheres 4 hours

after plating on adhesive substrate for the intermediate filament
\*\*\*nestin\*\*\* . Cells at the base of the sphere were placed in \*\*\*nestin\*\*\* . Cells at the base of the sphere were placed in plane of focus to illustrate filamentous staining. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of resulting spheres for 5 passages. (Scale bar 25 microns). FIG. 14 shows indirect immunofluorescence microscopy of a differentiated cell decorated with applieding against the eligedydday. cell decorated with antibodies against the oligodendrocyte progenitor marker 04. (Scale bar 12.5 microns).

FIG. 15 shows indirect immunofluorescence staining of a sphere 4 hours after plating on adhesive substrate for the intermediate filament vimentin. Cells at the base of the sphere were placed in plane of focus to illustrate filamentous staining. The sphere was generated by direct transfer of undifferentiated ES cells into serum free medium and propagation of resulting spheres for 7 passages. (Scale bar 25 microns). FIG. 16 shows the growth pattern of spheres that were generated directly from undifferentiated ES cells. Each bar represents the mean (+-SD)

derivation. A more excessive growth rate is evident during the first 5

FIG. 17 shows persistent growth in the volume of spheres along time. Each bar represents the mean (+-SD) increment in volume per week of 24 spheres at nine to twenty one weeks after derivation. The spheres were generated from differentiating ES colonies.

FIG. 18 shows linear correlation between the volume of spheres and the number of progenitor cells within a sphere. Spheres of various diameters, that were generated directly from undifferentiated ES cells and were propagated 5-7 weeks, were dissaggregated into single cell suspension and

the number of cells per sphere was counted. FIG. 19 shows RT-PCR analysis of gene expression in ES cells (a week after FIG. 19 shows RT-PCR analysis of gene expression in Es cells (a week arte passage) and neural spheres derived from differentiating colonies and directly from undifferentiated ES cell. All panels show 2% agarose gels stained with ethidium bromide. Lanes 1, 2 and 3, Oct-4 in ES cell culture, neural spheres derived from differentiating colonies, neural spheres derived from undifferentiated ES cells. Lane 4, stem cell culture, PCR for Oct-4 carried out with omission of reverse transcriptase. Lanes 5, 6, and 7, \*\*\*nestin\*\*\* in ES cell culture, neural spheres derived from differentiating colonies, neural spheres derived from undifferentiated ES cells. Lane 8, stem cell culture, PCR for \*\*\*nestin\*\*\* carried out with omission of reverse transcriptase \*\*\*nestin\*\*\* carried out with omission of reverse transcriptase. Lanes 9, 10 and 11, Pax-6 in ES cell culture, neural spheres derived from differentiating colonies, neural spheres derived from undifferentiated ES cells. Lane 12, stem cell culture, PCR for Pax-6 carried out with omission of reverse transcriptase. Lane 13, 100 bp DNA ladder. Oct-4 band is 320 bp, \*\*\*nestin\*\*\* is 208 bp and Pax-6 is 274 bp.
FIG. 20 shows indirect immunofluorescence microscopy of differentiated astrocyte cells decorated with antibody against \*\*\*GFAP\*\*\* (Scale

bar 25 microns)

FIG. 21 shows indirect immunofluorescence microscopy of brain sections of two mice (A and B) 4 weeks after transplantation of human neural precursors prelabeled with BrDU. Cells with a nucleus decorated with anti BrDU (brown stain, black arrow) are evident near the ventricular surface

(white arrow indicate mouse unstained nuclei, bar=20 microns).
FIG. 22 shows indirect immunofluorescence microscopy of brain sections of a mice 4 weeks after transplantation of human neural precursors prelabeled with BrDU. Wide spread distribution of transplanted human cells decorated by anti BrDU antibodies is evident in the periventricular areas. The periventricular area in A is demonstrated at a higher magnification in B and C. (Bars=150, 60 and 30 microns in A, B and C).

FIG. 23 shows indirect immunocytochemical microscopy of brain sections of a mice 4 weeks after transplantation of human neural precursors prelabeled with BrDU. The transplanted human cells are migrating along the rostral migratory stream (bar=150 microns).

FIG. 24 shows RT-PCR analysis of gene expression in neural spheres derived from differentiating (A) and undifferentiated (B) ES cells. All panels show 28 agarose gels stained with ethicium bromide Lanes 1 and 10 100 show 2% agarose gels stained with ethidium bromide. Lanes 1 and 10, 100 bpDNA ladder; Lane 2, CD34; Lane 3, Flk-1; lane 4, HNF-3; lane 5, alfafetoprotein. Lanes 6-9 PCR reaction on the same samples as lanes 2-5 carried out with the omission of reverse transcriptase. CD-34 band is 200 bp, Flk-1 is 199, HNF-3 is 390, AFP is 340 bp.
FIG. 25 shows by RT-PCR analysis the expression of \*\*\*GFAP\*\*\* and the plp gene in differentiated cells from neural spheres derived from

differentiating ES cell colonies. The expression of \*\*\*GFAP\*\*\* indicates differentiation into astrocytes while the presence of both dm-20 and plp transcripts indicate that differentiation into oligodendrocyte cells has occurred. Lanes 2,4,6 and lanes 3,5,7 are from two separate RNA samples from differentiated spheres that were independently derived from ES cells. Lane 1 and 8, 100 bp DNA ladder; Lanes 2 and 4, \*\*\*GFAP\*\*\*; lanes 3 and 5, plp and dm-20; lanes 6 and 7, PCR reaction on the same samples as lanes 3 and 5 carried out with the omission of reverse transcriptase. \*\*\*GFAP\*\*\* band is 383, plp band Lanes 2 and 4, omission of reverse transcriptase. is 354 bp and dm-20 is 249 bp.

FIG. 26 shows a dark field stereomicroscopic photograph of areas (arrows) destined to give rise to neural precursors in a differentiating ES cell

colony 3 weeks after passage (bar=1.6 mm). FIG. 27 shows indirect immunochemical analysis of marker expression in cultures of neurons derived from progenitor cells that were derived directly from undifferentiated ES cells: A, indirect immunofluorescence microscopy of neurits decorated with antibody against 160 kDa neruofilament protein. B and C, indirect immunofluorescence staining of differentiated cells for MAP2a+b and beta-tubulin III. Scale bars: A 100 microns, B and C 10 microns. FIG. 28 shows indirect immunochemical analysis of the expression of

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microns.
      FIG. 29 shows in vivo differentiation into astrocyte cells of transplanted
        human neural progenitors prelabeled with BrDU. Donor cells are identified
        by indirect immunochemical detection of BrDU (dark nuclei, arrows). Duel
        staining demonstrates donor cells decorated by anti
                                                                              ***GFAP***
      (orange). Transplanted cells are migrating into the brain parenchyma (white arrow) and are also found in the periventricular zone (dark arrow) (A), A higher magnification of cells that have differentiated into astrocytes and migrated into the host brain (B).

FIG. 30 shows in vivo differentiation into oligodendrocyte cells of transplanted human neural progenitors prelabeled with BrDU. Donor cells are identified by indirect immunochemical detection of BrDU (dark puclei
        are identified by indirect immunochemical detection of BrDU (dark nuclei,
        arrows). Duel staining demonstrates donor cells decorated by anti CNPase
        (orange). !
      ANSWER 140 OF 313
                              USPATFULL on STN
                                                                         DUPLICATE 37
         2002:294271
                         USPATFULL
         Cultures of human CNS neural stem cells
Carpenter, Melissa, Foster City, CA, UNITED STATES
                                 A1
                                        20021107
         US 2002164309
         US 6777233
                                        20040817
                                  B2
         US 2002-134234
                                 A1
                                        20020429 (10)
         Continuation of Ser. No. US 2000-486302, filed on 16 Oct 2000, PENDING A
         371 of International Ser. No. WO 1998-US18597, filed on 4 Sep 1998,
         UNKNOWN
         Utility
APPLICATION
LN.CNT
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INCL
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         INCLS: 435/368.000
         NCLM:
                  435/368.000
                  435/377.000
         NCLS:
         [7]
         ICM: C12N005-08
         ICS: A61K045-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 141 OF 313 USPATE 2002:265873 USPATFULL
                                                                         DUPLICATE 38
                               USPATFULL on STN
         DIAGNOSIS AND TREATMENT OF NEUROECTODERMAL TUMORS
         LYONS PH.D., SUSAN A., BIRMINGHAM, AL, UNITED STATES SONTHEIMER, HARALD W., BIRMINGHAM, AL, UNITED STATES
         US 2002146749
                                 A1
                                         20021010
             6667156
                                  B2
                                         20031223
         US 1999-296031
                                         19990421 (9)
                                 A1
         Utility
         APPLICATION
LN.CNT 977
INCL
         INCLM: 435/007.230
         INCLS: 435/007.100; 436/063.000; 436/064.000
         NCLM:
                  435/007.230
                  435/007.100; 436/063.000; 436/064.000; 436/813.000
         NCLS:
         [7]
         ICM: A61M036-14
         ICS: A61K051-00; G01N033-53; G01N033-574; G01N033-48
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 142 OF 313 USPATFULL on STN
                                                                         DUPLICATE 39
         2002:185669 USPATFULL
         Differentiated stem cells suitable for human therapy
         Gold, Joseph D., San Francisco, CA, UNITED STATES Lebkowski, Jane S., Portola Valley, CA, UNITED STATES
         US 2002098582
                                  Α1
                                         20020725
         US 6576464
                                         20030610
                                  B2
         US 2001-783203
                                  Α1
                                         20010213 (9)
         US 2000-253443P
                                   20001127 (60)
PRAI
         US 2000-253357P
                                   20001127 (60)
         Utility
         APPLICĂTION
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LN.CNT
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         INCLM: 435/366.000
         INCLS: 424/093.210; 435/194.000
         NCLM:
                  435/325.000
                  536/023.100; 536/023.400; 536/024.100; 536/025.500
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decorated with antibodies against tyrosine hydroxylase. Scale bars: 30

L5

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RLI

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ICM: A61K048-00
        ICS: C12N005-08; C12N009-12
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 143 OF 313 USPATFULL on STN
                                                                     DUPLICATE 40
        2002:72652 USPATFULL
AN
        Method for production of neuroblasts
Gage, Fred H., La Jolla, CA, UNITED STATES
Ray, Jasodhara, San Diego, CA, UNITED STATES
US 2002039789 A1 20020404
TI
IN
PΙ
        US 6599695
                                B2
                                      20030729
                                      20010724 (9)
AΙ
        US 2001-915229
                               A1
        Continuation of Ser. No. US 1997-884427, filed on 27 Jun 1997, GRANTED, Pat. No. US 6265175 Continuation of Ser. No. US 1995-445075, filed on 19 May 1995, ABANDONED Division of Ser. No. US 1993-147843, filed on 3 Nov
RLI
        1993, GRANTED, Pat. No. US 5766948 Continuation-in-part of Ser. No. US
        1993-1543, filed on 6 Jan 1993, ABANDONED
DT
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                 435/006.000; 435/007.100; 435/007.200; 435/007.210; 435/029.000
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IC
        [7]
        ICM: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
                             BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
       ANSWER 144 OF 313
                    BIOTECHDS
       2003-09341
AN
TI
       Generating substantially homogeneous population of undifferentiated cells
       from sample, by disrupting tissue sample, discriminating cells in
       population based on size and performing cell-surface marker-
       discrimination;
           for tissue engineering and gene therapy
ΑU
       BARTLETT P F; RIETZE R L
       HALL INST MEDICAL RES WALTER and ELIZA
PA
       WO 2002097067 5 Dec 2002
PI
       WO 2002-AU700 31 May 2002
AI
PRAI
       AU 2001-5403 1 Jun 2001; AU 2001-5403 1 Jun 2001
DT
       Patent
LΑ
       English
       WPĪ: 2003-140465 [13]
OS
L5
      ANSWER 145 OF 313 USPATFULL on STN
                        USPATFULL
        2002:337936
AN
TI
        TGF-alpha polypeptides, functional fragments and methods of use therefor
        Twardzik, Daniel R., Bainbridge Island, WA, UNITED STATES
TN
        Pernet, Andre, Lake Forest, IL, UNITED STATES Felker, Thomas S., Vashon, WA, UNITED STATES
                   Stefan, Bainbridge Island, WA, UNITED STATES
        Paskell,
PA
        Stem Cell Pharmaceuticals, Inc. (U.S. corporation)
        US 2002193301
US 2002-39119
PΙ
                                Α1
                                      20021219
AI
                               A1
                                      20020104 (10)
        Continuation of Ser. No. US 2000-641587, filed on 17 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-492935, filed on 27 Jan 2000,
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        PENDING Continuation-in-part of Ser. No. US 1999-378567, filed on 19 Aug
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        ICM: A61K038-18
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 146 OF 313
L5
                             USPATFULL on STN
AN
        2002:322564 USPATFULL
TI
        Method for transdifferentiation of non pancreatic stem cells to the
        pancreatic differentiation pathway
        Ramiya, Vijayakumar, Gainesville, FL, UNITED STATES
Clark, Amy, Gainesville, FL, UNITED STATES
IN
        US 2002182728
US 2002-113118
PI
                                      20021205
                                A1
AI
                                Α1
                                      20020329
                                                 (10)
PRAI
        US 2001-279922P
                                 20010329 (60)
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FS
         APPLICATION
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         INCLM: 435/366.000
         INCLS: 424/093.210; 424/093.700
NCLM: 435/366.000
NCL
         NCLM:
                  424/093.210; 424/093.700
IC
         [7]
         ICM: A61K048-00
         ICS: C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      ANSWER 147 OF 313
L5
                               USPATFULL on STN
ΑN
         2002:315966
                         USPATFULL
ΤI
         Transgenic mice expressing fluorescent protein
         Enikolopov, Grigori N., Cold Spring Harbor, NY, UNITED STATES Mignone, John, Bronxville, NY, UNITED STATES Cold Spring Harbor Laboratory (U.S. corporation)
IN
PA
PI
         US 2002178460
                                         20021128
                                  A1
ΑI
         US 2002-150509
                                  A1
                                         20020516
                                                     (10)
         Continuation of Ser. No. WO 2000-US31150, filed on 14 Nov 2000, PENDING
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 148 OF 313 USPATFULL on STN
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AN
         2002:301574
         TGF-alpha polypeptides, functional fragments and methods of Twardzik, Daniel R., Bainbridge Island, WA, UNITED STATES Pernet, Andre, Lake Forest, IL, UNITED STATES Felker, Thomas S., Vashon, WA, UNITED STATES
TI
                                        functional fragments and methods of use therefor
IN
         Paskell, Stefan, Bainbridge Island, WA, UNITED STATES
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         US 2002169119
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ΑI
         US 2001-932172
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                                         20010817 (9)
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         ICM: A61K038-18
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L5
      ANSWER 149 OF 313
                               USPATFULL on STN
AN
         2002:301223 USPATFULL
TI
         Method of isolating human neuroepithelial precursor cells from human
         fetal tissue
        Mayer-Proschel, Margot, Pittsford, NY, UNITED STATES Rao, Mahendra S., Salt Lake City, UT, UNITED STATES Tresco, Patrick A., Sandy, UT, UNITED STATES Messina, Darin J., Salt Lake City, UT, UNITED STATES
IN
PΙ
         US 2002168767
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         US 2001-813429
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         NCLS:
                  800/008.000
IC
         [7]
         ICM: C12N005-08
         ICS: A01K067-00
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ANSWER 150 OF 313

USPATFULL on STN